Tinnitus and Patterns of

Hearing Loss

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Abstract

This study investigates the differences in cochlear function present in two hearing-impaired groups; one with tinnitus and the other without tinnitus. The presence of tinnitus is closely linked with hearing impairment. However, it is still not clear why only some people with hearing impairment perceive tinnitus. One possibility is that tinnitus sufferers have specific hearing defects that are not found in hearing-impaired listeners without tinnitus. This leads on to the prospect of two *distinct* classes of hearing impairment; one with tinnitus and the other without. Few studies investigated this possibility because most studies concentrated on the gross differences between tinnitus and no tinnitus groups, irrespective of hearing impairment. Behavioural measures of cochlear function was compared by using measures of (1) absolute thresholds, (2) frequency selectivity, (3) cochlear compression, (4) uncomfortable loudness levels (ULLs) and (5) distortion products otoacoustic emission (DPOAEs). The assumption that *all* hearing-impaired individuals have similar amounts of reduced frequency selectivity and loss of compression was *not* observed in this study. Tinnitus sufferers were observed to have (1) steeper slopes in the audiograms, (2) larger threshold duration differences, (3) less off-frequency listening, (4) better frequency selectivity and (5) stronger presence of compression than listeners who had similarly raised thresholds, but no tinnitus. No significant differences were found with discomfort level or DPOAE responses. The patterns of results are consistent with inner hair cell dysfunction, and not outer hair cell damage, as previously suspected. This supports deafferentation theories postulated by Bauer et al. (2007). The existence of two distinct classes of hearing impairment, also suggests the need for different hearing-aid strategies for the two groups. The simple use of the presence of tinnitus as a marker for the type of hearing-impairment suffered may improve the way hearing-aids are prescribed.

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List of Abbreviations

AN	Auditory nerve
C.I.	Confidence Interval
DCN	Dorsal Cochlear Nucleus
DPOAE	Distortion Products Otoacoustic Emission
F_{dp}	Frequency at measured DPOAE
F_p	Probe frequency
GUI	Graphical User Interface
HF	High-frequency
HSR	High spontaneous rates
Hz	Hertz
IFMC	Iso-Forward Masking Contour
IHC	Inner hair cell
LF	Low-frequency
MMF	Minimum masked frequency
msec	milliseconds
OHC	Outer hair cell
PTC	Psychophysical Tuning Curve
RETSPL	Reference Equivalent Threshold Sound Pressure Level
SOAE	Spontaneous Otoacoustic Emission
SL	Sensation Level
THI	Tinnitus Handicap Inventory
TMC	Temporal Masking Curves
TMMC	Tinnitus Modulation Manoeuvre Checklist
TS	Tinnitus Spectrum
TTS	Temporary Threshold Shifts
ULL	Uncomfortable Loudness Level

Chapter 1
Introduction

The precise triggers of tinnitus are still unknown. Most tinnitus sufferers have damaged hearing, but it is not understood why only a *proportion* of hearing-impaired people perceive tinnitus. This question has never been thoroughly addressed as most studies concentrated on the gross differences between tinnitus and no tinnitus group regardless of hearing levels. This study aims to identify the differences in cochlear function between tinnitus and no tinnitus group with similarly impaired thresholds. The presence of these differences will highlight specific patterns of inner ear damage that trigger tinnitus.

This first chapter introduces the importance and complexities of tinnitus research. The perception of tinnitus has been a part of medical history as far back as the seventh century B.C. (Stephens, 2000). In 1981, the CIBA Foundation held the first tinnitus symposium to highlight the need to better understand the condition (Ciba, 1981). Presently, the exact mechanisms that trigger tinnitus are still unknown, and as such, tinnitus rehabilitation is relegated to treating the symptoms and not the actual mechanisms that cause it in the first place.

Tinnitus is a growing cause for concern because it affects between 10% to 15% of the adult population in the UK (Hoffman and Reed, 2004). The prevalence of tinnitus can be as high as 30% if the criteria of tinnitus was relaxed to include temporary tinnitus triggered by the common cold (Davis and El Refaie, 2000). The persistence of tinnitus affects sleep patterns, anxiety levels and impacts greatly on the overall quality of life (El Refaie et al., 2004).

1.1   The need for better classification of tinnitus

Tinnitus research is further complicated by a variety of conditions that are associated with it. Tinnitus is recognised as a symptom, not a disease, and is commonly described as the perception of sound in the absence of any external stimuli (Ciba, 1981). This means an assortment of defects may trigger tinnitus, some auditory, while others involve somatosensory defects (Levine, 1999). Some authors (Hazell, 1995; McFadden, 1982; Møller, 2007) have proposed dual categories of tinnitus, such as *objective*/ *subjective* tinnitus. *Objective* tinnitus includes sounds that were created internally by the body, for instance, pulsations, palatal and intra-tympanic myoclonus, the jugular outflow syndrome and so on. Subjective tinnitus, on the other hand, is attributed to abnormal neural activity along the auditory pathway and beyond. Although some forms of *objective* tinnitus can be treated and sometimes eradicated completely, *subjective* tinnitus is more complicated and the wide number of aetiologies that are associated with it, results in an abundance of possible theories that explain its mechanism.

Other classifications of tinnitus include *peripheral*/ *central* tinnitus (Fowler, 1939). This classification was an attempt to identify the locus of tinnitus generation. *Peripheral* models of tinnitus generation commonly included the outer/ middle ear and cochlea, where damage to the biochemical balance, transduction processes or mechanical motion of the structures in the cochlea were hypothesised to generate the perception of tinnitus (Baguley, 2002). *Central* tinnitus was used to describe instances of persistent tinnitus that happen post-cochlear ablation. Tinnitus was then thought to be generated by central structures in the absence of a peripheral source (Ciba, 1981).

Other authors, however, rejected these dual classifications of tinnitus because the categories were not defined in a sufficiently specific manner and were not mutually exclusive. Hazell (1995) and Jastreboff (1995) proposed that tinnitus should be defined according to the

possible defects that are suspected to trigger the condition. These included, for instance, tinnitus caused by somatosounds, Eustachian tube-tinnitus, Vestibular schwannoma-tinnitus, cortical-tinnitus and so on. Savastano (2004) echoed this need for proper classification, noting that most of the data collected on tinnitus consisted of questionnaires that were mailed out to patients who had tinnitus, without considering the types of tinnitus they had, or if it was related to other otologic symptoms. Indeed, tinnitus presents itself as a symptom, rather than a diagnostic entity, therefore the ability to distinguish between the many types of tinnitus should precede research on its treatment (Coles, 1995; Møller, 2007).

This study aims to concentrate on a specific form of tinnitus that is triggered by damage to the inner ear, defined in this study as *cochlear tinnitus* (Section 2.1). Strict screening procedures were set in place to screen for other forms of tinnitus that are triggered by non-auditory pathologies (Section 3.3). These types of non-auditory tinnitus were not included in the main analyses, but are introduced as case studies in Appendix I.

1.2 The relationship between hearing damage and tinnitus

The presence of tinnitus is normally associated with some form of impairment along the auditory pathway. This has been demonstrated in various clinical studies that reported tinnitus in people with known hearing disorders such as otosclerosis, noise-induced hearing disorders and presbycusis (Davis and El Refaie, 2000; Davis, 1989). The relationship between hearing impairment and tinnitus is further complicated by reports that people with *clinically normal-hearing* also suffer from tinnitus (Schaette and McAlpine, 2011; Shiomi et al., 1997). The term 'normal-hearing' in most studies is in reference to the listening ability of young adults without known hearing problems (BSI, 2004). Subsequent research suggested that this population of tinnitus sufferers may have undetected hearing impairment that is not revealed by the

audiogram. Impairments to either of the cochlear hair cell systems have been suggested to occur in people who have clinically normal-hearing, but also perceive tinnitus (Shiomi et al., 1997; Weisz et al., 2006). However, although *any* damage to structures in the inner ear may result in impaired hearing, it is still unknown what specific defects in the inner ear uniquely trigger the perception of tinnitus in only a proportion of hearing-impaired listeners.

Only some of the early theories on tinnitus attempted to explain the absence of tinnitus in hearing impairment. The discordant damage theory (Section 2.1.3) proposed that selective *imbalance* between damage to type I and type II fibres (which relates to inner and outer hair cell damage) is detected by a central comparator and interpreted as phantom sound. If both systems are equally damaged, however, the balance is not disrupted and no tinnitus is perceived. The edge theory (Section 2.2) suggests that abnormal synchrony of the auditory nerve firing rates, caused by damage to the periphery happens in people with tinnitus. The abnormal patterns of firing rates are interpreted by the brain as phantom sound.

Epidemiological studies have provided an insight into the proportion of people who suffer from tinnitus. Sanchez's (2004) report, for instance, summarises a number of epidemiological studies and reports tinnitus prevalence between 8% to 30% across the studies that were reviewed. The Medical Research Council's Institute of Hearing Research (1981) reported the presence of tinnitus in about 9% of their questionnaire respondents (across 4 cities in the United Kingdom). About 8.5% of the respondents reported both hearing impairment and tinnitus and 17% reported to have impaired hearing, although it is not clear if this includes those who also have tinnitus. There was a consistent trend in Sindhusake et al.'s (2003) report that suggested higher audiometric thresholds (worse hearing) in hearing-impaired listeners with tinnitus compared to those with only a hearing impairment. None of the

studies that were reviewed explicitly compared the proportion of hearing-impaired listeners

with tinnitus and those who were hearing-impaired but did not have tinnitus.

The aim of this study is to uncover the presence of unique defects in the cochlea that

may trigger the perception of tinnitus. This is achieved by studying the differences in cochlear

function between groups of people with hearing impairment, but with and without tinnitus

(Chapter 5 to Chapter 12). The original proposal of the study was open to all possibilities, as

there were no known preceding studies of this nature. However, the accumulation of results

obtained at the end of the study, points to distinct patterns of hearing that are unique in only

the hearing-impaired population with tinnitus.

1.3   Psychophysical measurements of hearing

Audiometry is the most common method used to assess the fidelity of the whole

auditory system. However, it does not provide site specific information about damage that may

happen in the inner ear (Weisz et al., 2006). This makes it difficult to draw parallels between

human data and that of animal studies, which provide more extensive insights on site-specific

defects that occur in the inner ear.

Psychoacoustic measurements are not commonly performed clinically as it is time

consuming and require a substantial amount of training. However, they are valuable tools that

are used to investigate the fidelity of cochlear function. Psychoacoustical measurements like

the Psychophysical Tuning Curve (PTC) have been suggested to provide information about the

function of the hair cells in the cochlea (Kluk and Moore, 2005; Moore and Alcantara, 2001).

The Hearing Research Lab at the University of Essex developed the concept of

measuring Hearing Profiles (Meddis et al., 2010). These profiles are a set of psychophysical

measurements, which include measures of absolute thresholds, frequency selectivity and

compression. These tests were devised with speed and efficiency in mind, whilst maintaining

the amount of information it provided on the integrity of cochlear function. The paradigm used

in these tasks was the cued single-interval adaptive procedure (Lecluyse and Meddis, 2009).

The method allowed measurement time to be substantially reduced. It is possible to obtain a

full Hearing Profile (with measurements at 5 frequencies) under 2 hours with minimal amounts

of training (Lecluyse and Meddis, 2009), and (Lecluyse, personal communication).

The main benefit of these Hearing Profiles is the creation of 'Hearing Dummies', or

computer models of a person's hearing. These models can then be used to infer the pathologies

that cause a person's hearing loss, and used to determine suitability of subsequent

rehabilitative methods (Panda, 2010). The first stage in this process is to develop a computer

model of normal-hearing. Hearing impairment can then be modelled by specific adjustments

made to a series of parameters that relate to different stages in the auditory pathway. Various

hearing-aid strategies can then be tested on this computer model to identify which strategy

provides the greatest benefit. This can all be achieved before the hearing-impaired individual is

provided with an actual hearing-aid prescription, this saving time on recurring hearing-aid

reprogramming sessions.

The Hearing Profiles in this study were modified to include additional quantitative

measures of tinnitus. The Tinnitus Spectrum method was preferred to the more traditional

method of measuring tinnitus pitch, which has high within- and between-session variability

(Penner, 1983). The very subjective nature of the tinnitus and its non-stable character has been

stipulated to be a cause of this high variability. There is also an inherent difficulty of matching

tinnitus sounds of variable sound qualities (buzzing, hissing and so on) to pure tones. In the

Tinnitus Spectrum task (Noreña et al., 2002), participants were asked to rate (on a scale of 0 to

10) the contributions of pure tones to the overall percept of tinnitus. The results produce a

tinnitus 'spectrum' that has been shown to be inversely related to the amount of hearing loss (Chapter 5). Pure tones that were given high ratings coincided with areas in the audiogram that suffered the most impairment. The suitability and robustness of this method to detect a simulated pure tone sound was investigated in normal-hearing individuals before using the method on people with tinnitus (Section 3.4.6).

This study implements psychophysical methods to obtain a Hearing Profile in order to compare the differences in cochlear function between the two hearing-impaired groups. The methods used are automated and requires minimal practice. A full Hearing Profile can be obtained within a day. Sixty-nine participants in total were tested using the method (Chapter 4, Appendix G). This was three times the number of participants estimated that were originally. The statistical analyses performed had to take into account the unequal sample size in each group (for example, Levene's test to check if variances in each group is equal, and Welch's t-test or Brown-Forsythe test to compare two population means).

1.4 Clinical Implications

Firstly, clear distinctions between the hearing-impaired groups would suggest that the perception of non-pathological tinnitus can be used to predict the type of cochlear function present hearing impairment. The presence of differences in cochlear function would mean that the cochlea processes sounds differently between the two hearing-impaired groups. This information can then be used to predict outcomes of aural rehabilitative methods. Secondly, a greater understanding about the conditions that trigger tinnitus may help future research make better progress to help alleviate this debilitating condition. This can be done by improving the way computer models predict the conditions that trigger tinnitus. Thirdly, knowledge on the

initial defects that are responsible for activating the perception will lead to new ideas and

innovative precautionary methods to prevent tinnitus from being established in the first place.

Chapter 2
Literature Review

This chapter reviews the theories associated with tinnitus that may be triggered by cochlear damage (further defined in this chapter as *cochlear tinnitus*). This includes (1) the different types of micro structural damage that happen in the cochlea, (2) the tinnitus theories associated with them and (3) the psychophysical measurements used to detect these defects. Tinnitus sufferers often have impaired hearing. This is true even in tinnitus sufferers with seemingly normal-hearing. Studies report the presence of previously undetected cochlear damage in this population (Ozimek et al., 2006; Shiomi et al., 1997; Weisz et al., 2006), which further strengthens the connection between tinnitus and cochlear damage.

2.1   'Cochlear' tinnitus

2.1.1   Definition

The classification of tinnitus has been subjected to debate by various authors (Coles, 1995; Jastreboff, 1995; Møller, 2007). This reflects yet another complication of tinnitus; the inability to objectively distinguish between the many triggers that are associated with it. Møller (2007) asserts that the search for a single cure for tinnitus is futile so long as it is not possible to make distinctions between the many forms of tinnitus.

It is therefore important to classify the presence of tinnitus in terms of the damage to the structures that are responsible for triggering it. This study hypothesises that *specific cochlear damage* triggers the perception of tinnitus, termed *'cochlear tinnitus'*. In this study, therefore, strict measures were put in place to include human participants with only suspected

cochlear damage that may act as a trigger for tinnitus. The definition of *cochlear tinnitus* is important at this point as other non-auditory pathologies (temporomandibular joint disorders or head and neck injuries), or outer- and middle ear damage (otosclerosis) are also associated with tinnitus (Chole and Parker, 1992; Gristwood and Venables, 2003). These types of non-cochlear tinnitus are excluded from the main study, and these include those of known pathological origin, such as pulsing tinnitus (caused by vascular pathologies), or other forms of tinnitus with known associated conditions such as Ménière's Disease, or vestibular schwannoma.

Temporary sensations of tinnitus are also excluded from the main study, because it is not clear whether they would have the same inner ear damage suffered as those with *permanent* tinnitus. This is because temporary tinnitus can happen after intense exposure to noise, and has the ability to disappear in some instances (Atherley et al., 1968; Loeb and Smith, 1967). This is not the case for people who have a constant perception of tinnitus.

Cochlear tinnitus in this study is defined as (1) the *permanent* (continuous) perception of phantom sound in the absence of any external stimuli that (2) is present in all kinds of acoustic environments, and (3) not associated with known medical conditions, such as, acoustic neuroma or Ménière's Disease. Participants with tinnitus that do not meet this definition are presented as individual case studies in Appendix H and Appendix I.

2.1.2   Cochlear damage

Cochlear damage caused by excessive noise exposure has been demonstrated to be associated with both hearing impairment and tinnitus (Axelsson and Prasher, 2000; Loeb and Smith, 1967). Histopathological studies have shown that damaged hearing can be caused by damaged structures in the cochlea (Kujawa and Liberman, 2009; Nordmann et al., 2000). These

may affect a number of processes in the cochlea. This includes damage to microstructures on

the hair cells (e.g. stereocilia), the hair cells themselves and other processes beyond the hair
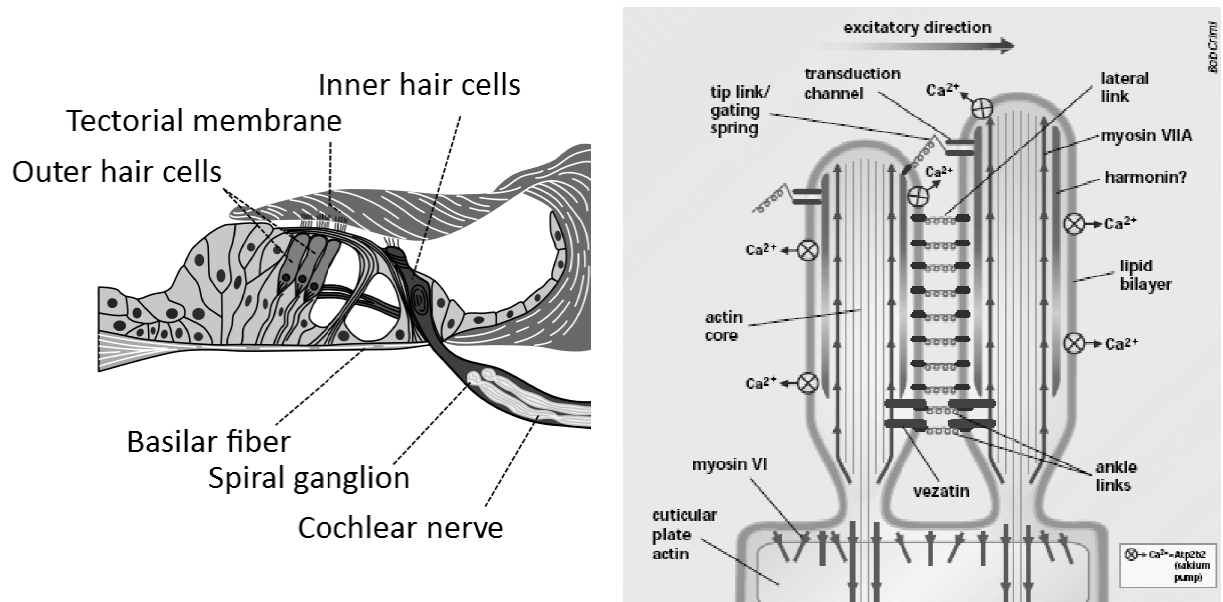
cells (Figure 2.1).

Figure 2.1: Schematic diagrams of the Organ of Corti (left) and the stereocilia located at the top of the hair cells (right), figure adapted from Steel et al. (2001).

Damage to micro structures, such as the stereocilia and the tip-links between the

stereocilia, can happen prior to damage to the hair cells themselves; the stereocilia can become

disarrayed or even fused to each other (Liberman and Dodds, 1984; Nordmann et al., 2000;

Wang et al., 2002). Damage to the tip-links *between* the stereocilia, however, happen on

normal-looking stereocilia, suggesting that they are more vulnerable to trauma (Pickles et al.,

1987). Breakage of side links between the cytoskeleton and the stereocilium can also result in

fractured tip-links. Tip-link damage can impact on the structure of the stereocilia itself, causing

eventual disarray (Pickles et al., 1987). There is evidence that mammalian tip-links between the

stereocilia have the ability to self-repair. This tip-link regeneration commonly occurs within 24

hours and has been implicated in the recovery from temporary threshold shifts (Jia et al., 2009).

There are currently no reports of the regeneration of stereocilia or hair cells in the mammalian cochlea.

At present, there is no known research that investigates the relationship between damaged tip-links and the presence of temporary tinnitus. However, the time scale of tip-link recovery is comparable to the time scale of temporary tinnitus after loud noise exposure, and it is highly likely that the two may be related. Tip-links are thought to act as gated springs that are responsible for mediating the transduction process. Excitotoxicity due to biochemical imbalance in the cells may be a result of these damaged tip-links. Excessive stimulation due to excitotoxicity could result in hyperactivity in central structures and perceived as sound. Self-recovery of these tip-links, after 24 hours, may alleviate this form of tinnitus, by restoring the biochemical imbalance of the cells affected.

Early histopathological studies often observed that outer hair cells were more susceptible to damage compared to inner hair cells (Hawkins, 1973; Morest and Bohne, 1983). This belief has formed the foundation for a multitude of theories relating to tinnitus and the way hearing-impaired people process sounds (Jastreboff, 1995; Moore, 2004a). More recent research, however, challenge the belief that outer hair cells are more vulnerable to damage compared to the inner hair cells. Kujawa and Liberman (2009) studied the effects of neural degeneration in mice that suffered from noise-induced temporary shifts (TTS). The authors observed the irreversible loss of synaptic ribbons located at the base of the inner hair cells. This led to the progressive loss of auditory fibres over several months despite possessing normal outer hair cell function. The synaptic ribbons maintain tonic neurotransmitter release to the auditory fibres and are important for fast and synchronous release of neurotransmitters (Schmitz, 2009).

The loss of these synaptic ribbons did not prevent hearing thresholds from returning to normal after temporary threshold shifts. Kujawa and Liberman (2009) hypothesised that threshold recovery is possible if the remaining auditory fibres compensate the loss by increasing the discharge rate or by increasing the number of fibres that respond to stimulation. The authors suggested that degradation of auditory fibres lead to cortical reorganisation, which may explain the presence of tinnitus. This supports the general theory of deafferentation as a trigger for tinnitus, and is discussed in Section 2.3.

The mechanisms of tinnitus-inducing ototoxic drugs such as salicylates, loop diuretics, quinine, carboplatin and furosemide have also been investigated. Salicylates, such as aspirin, was thought to preferentially affect the outer hair cells (Brownell, 1990), but later studies reported damage to spiral ganglion cells that resulted in subsequent neural degeneration (Peng et al., 2003). Quinine, also a tinnitus-inducing drug, causes a decrease in auditory fibres without affecting the neural tuning curves. This suggestion that outer hair cell function was preserved post quinine poisoning (Mulheran, 1999), was in contrast to Jarboe et al.'s (1999) observation of reduced outer hair cell responses. The differences between the two studies could be accounted for by the different methodologies used. Mulheran (1999) made *in vivo* measurements, while Jarboe et al. (1999) made *in vitro* measurements. In vitro measurements may not accurately represent processes that correct for biochemical imbalance in affected cells. Furosemide, another tinnitus-inducing drug, is known to decrease endocochlear potential and has been used in numerous studies to mimic the effects of presbycusis. Observations by Sewell (1984b), for instance, showed that furosemide had a greater detrimental effect on the inner, rather than the outer hair cells. Carboplatin, which also triggers tinnitus, selectively disrupts inner hair cell function while allowing for normal outer hair cell function (Wake et al., 1994; Wang et al., 1997).

In summary, tinnitus-inducing processes, whether by noise trauma or by pharmaceutical means, affect a variety of structures in the inner ear, some of which have yet to be reported. Any damage to the structures in the inner ear may cause reduced hearing, but the exact site of damage that triggers tinnitus is still unknown.

2.1.3 Theories based on cochlear damage

LePage (1995) proposed that disarrayed stereocilia on the inner hair cells may result in constant deflection of the stereocilia and a change or a drift in the operating point of the cell. The result of this constant discharge is tinnitus. Zenner et al. (1993), however, suggested that pathological deflections of the inner hair cell's (IHC) stereocilia or ion disorders of the cell changes the receptor potential of the cell. This causes the cell to release neurotransmitters at an abnormal rate, which also changes the spontaneous activity at the cochlear nerve attached to it. The change of pattern in activity is perceived as tinnitus, as first suggested by Kiang et al. (1970).

Tonndorf (1981) suggested that decoupling of hair cells from the tectorial membrane may generate tinnitus. He suggested that a low-level noise existed in all substances due to the random motion of molecules as explained by Brownian motion theory. Tight coupling between the stereocilia and the tectorial membrane would result in lower mean velocity of particles between the two and therefore lower noise levels. Partial decoupling, on the other hand, would increase the velocity of particles and the level of noise, which is then perceived as tinnitus. Tonndorf's (1981) theory would only implicate the outer hair cells, because the stereocilia of the outer hair cells (OHCs) are embedded in the tectorial membrane, whereas the stereocilia of the inner hair cells (IHCs) are not (Hoshino, 1977; Kimura, 1966). Later publications by the

author did not specify the extent of 'ciliary dysfunction' that is thought to trigger tinnitus or the specific types of hair cell systems that may be implicated in the theory.

Jastreboff (1990) introduced the theory of discordant damage to explain the presence (and absence) of tinnitus in individuals with damaged hearing. The discordant damage theory relates to dysfunction of both Types I and II afferent fibres in the auditory nerve. About 20 Type I fibres innervate each IHC, whilst about 6 Type II fibres innervate each OHC. Type I fibres are bipolar, myelinated, driven by tones and display high levels of spontaneous activity. Type II fibres are monopolar and unmyelinated. The literature to date have reported responses to acoustic stimulation in Type I fibres, but not in the unmyelinated Type II fibres. It is unclear what role these Type II fibres play in the perception of hearing. Both Type I and II fibres project onto the cochlear nucleus (Pickles, 2008).

Jastreboff (1990) proposed that uneven damage to the OHC and IHC systems will result in imbalanced activity between the Type I and II fibres. This in turn causes disinhibition at the level of the dorsal cochlear nucleus (DCN) and the hyperactivity that results from this is interpreted as tinnitus. The theory revolves around early physiological observation that OHCs were more vulnerable to noise damage compared to IHCs (Hawkins, 1973). Jastreboff (1990) also explains that because the discordant theory hinges upon the imbalance between the OHC and IHC systems, individuals with *equally* damaged systems will only experience a hearing problem and will not perceive tinnitus. Jastreboff (1990) also suggested that it was possible to have seemingly normal audiogram and yet experience tinnitus. This was in reference to Clark et al.'s (1984) suggestion that OHC damage as much as 30%, if relatively homogenous, may not be detected in an audiogram.

In summary, the theories based in cochlear damage suggest both the outer and inner hair cell systems as possible triggers of tinnitus. However, the theories preferentially suggest

outer hair cell damage to be the main cause of tinnitus because of its possible vulnerability to damage.

2.2   The 'Edge Effect' Theory and role of Spontaneous Activity

The 'Edge Effect' Theory is based on clinical observations that tinnitus sufferers often had high-frequency hearing loss and that the pitch of tinnitus is perceived close to the frequency region where hearing loss begins (Fowler, 1942; Josephson, 1931; Mortimer et al., 1940; Wegel, 1931). Kiang et al. (1970) attempted to explain this phenomenon in terms of spontaneous activity present in the auditory nerve. The authors studied the amount of spontaneous activity of the auditory nerve (AN) in cats with normal and abnormal cochleae. The cats were administered with kanamycin, and suffered damage to both outer and inner hair cell systems. This resulted in a decrease in spontaneous activity of the auditory nerve. Kiang et al. (1970) hypothesised that the absence of *normal* pattern of spontaneous activity results in a subjective perception of sound. They proposed a central monitoring comparator that is sensitive to differential inputs from the periphery. The authors suggested that spontaneous activity is not normally heard because the perception of sound depends on synchronous firing of neighbouring neurons. Under normal spontaneous conditions, there is an *absence* of neural synchrony in the AN. However, when part of the periphery is impaired, the pattern of input to the comparator is affected. This change in the *pattern* of spontaneous activity is perceived by the brain as sound. It is still not known what, or how much damage is necessary to cause such a pattern shift in spontaneous activity. However, it was suggested that this change in spontaneous activity is triggered by a sharp decline in thresholds that relate to areas in the cochlea where functioning hair cells are located adjacent to (or at the 'edge' of) abnormal or missing ones (Kiang et al., 1970; Liberman and Kiang, 1978).

This 'Edge Effect' theory predicts that the pitch of the tinnitus will happen in the region where this steep decline occurs. The hypothesis appealed to clinical evidence that reported sharply-sloping high-frequency loss in those who perceived tinnitus. However, it does not account for individuals with shallower-sloping losses who also perceived tinnitus, or explained the occurrence of other groups of people with sharply-sloping losses who *do not have tinnitus* (Meikle and Taylor-Walsh, 1984). The 'Edge Effect' theory is supported by observations of changes in the tonotopic representation of sounds in the auditory cortex (Eggermont and Roberts, 2004; Noreña et al., 2003). Plastic changes that occurred in acoustically traumatised animals resulted in an over-representation of the 'edge' frequency. This change in tonotopic arrangement is thought to occur with weakening inhibition, which leads to the perception of phantom sound. However, why it should only occur in a subpopulation of people with hearing impairment is still unknown.

Hazell (1987) extended the 'Edge Effect' hypothesis to include the effects from the efferent system. He hypothesised that at this 'edge', an overshooting of the efferent stimulation of normal outer hair cells (OHCs) adjacent to abnormal ones can happen. The ratio of efferent innervation is roughly 1 fibre to 50 OHCs. This means that it is possible for the OHCs along these 'edge' areas to be exposed to inappropriate disinhibition by the efferent system, leading to over excitation of neurons and the perception of tinnitus.

Hazell's (1987) theory accommodates some clinical observations relating the presence of tinnitus pitch that happen at the start of the slope of the audiogram. However, the theory suggests that a lack of disinhibition would result in excitation at the level of the cochlea. This contradicts previous observations that reported no increase in spontaneous activity in the auditory nerve (Kiang et al., 1970). It has also been suggested that Hazell's (1987) model of over excitation of the OHCs would result in high levels of recordable spontaneous emissions from

the cochlea (Jastreboff, 1995). This has not shown to be the case because most people with tinnitus have some form of hearing impairment and do not have recordable spontaneous otoacoustic emissions (SOAEs). However, Penner (2000) argues that this may be a consequence of measurement limitation rather than an absence per se.

Kaltenbach and colleagues (1992; 2005; 2002) investigated changes in spontaneous activity in the dorsal cochlear nucleus (DCN). Noise trauma and cisplatin, a known anticancer drug which also induces tinnitus, were both used separately to induce tinnitus. The authors observed an increase in spontaneous activity (hyperactivity) in the dorsal cochlear nucleus in both separate experiments. This *hyperactivity* is suggested to be a neural correlate of tinnitus. Zacharek et al. (2002) showed that the hyperactivity persisted even after cochlear ablation, which suggested that it was not generated within the cochlea, rather, it may have been generated in more central regions.

Plastic readjustments have been suggested to play an important role in maintaining this hyperactivity. Kaltenbach and colleagues (1992; 2005; 2002) reported a decrease in spontaneous activity in the DCN immediately after cochlear insult (2 days), but a gradual build up of hyperactivity 5 days after the exposure, which then persisted after 30 days. Brozoski et al. (2005) demonstrated that ablation of the dorsal cochlear nucleus did not decrease the perception of tinnitus in rats, rather, increased it. This suggests that cochlear damage, which triggers the hyperactivity in the dorsal cochlear nucleus, may be propagated and maintained by central structures further along the hearing pathway.

In summary, tinnitus theories have been proposed to be linked to (1) spontaneous activity in the auditory nerve, (2) spontaneous emissions from the cochlea and (3) spontaneous activity in the dorsal cochlea nucleus. However, the recurring complication of explaining why these processes may be unique to *only* people with tinnitus, remain absent.

2.3   General deafferentation theory

The deafferentation theory was adapted from pain and phantom limb studies, and centres around the ability of the brain to adapt to loss of input (Folmer et al., 2001). Imaging studies first reported changes in the tonotopic frequency representation in the brain after hearing was damaged (Adjamian et al., 2009; Dietrich et al., 2001; Eggermont and Roberts, 2004). This plastic ability has been theorised to be essential in maintaining the perception of tinnitus. Studies in smaller mammals showed that damage to the auditory periphery (which led to subsequent deafferentation) decreased innervation to the granule cell region of the cochlear nucleus. This leads to compensatory cross modal innervation in the deafferented region, which disrupts the balance between excitatory and inhibitory inputs, resulting in plastic changes and the perception of tinnitus (Shore, 2004).

The general deafferentation theory links cochlear damage to plastic changes in central structures, which trigger and possibly maintain the perception of tinnitus. The theory suggests that people who have loss or reduced input to central structures are more at risk of developing tinnitus. It implicates that damage to both outer and inner hair systems, which reduces acoustically-driven input from the periphery, has the potential of causing these plastic changes. This has been hypothesised from animal models (either traumatised by noise or ototoxic drugs) that reveal damage to a combination of the outer and inner hair cell systems, the spiral ganglion cells and the endocochlear potential (Mulheran, 1999; Nordmann et al., 2000; Peng et al., 2003; van Ruijven et al., 2005).

The main caveat in the deafferentation theory is that it enforces the misconception that everyone who is hearing-impaired will have tinnitus. This is not true. The only known study that attempted to explain the role of deafferentation in people who were hearing-impaired, but yet do not perceive tinnitus, was conducted by Bauer at al. (2007). The authors exposed rats to

noise trauma, using moderately loud stimuli that resulted in minimal outer and inner hair cell damage. There was a low correlation between the behavioural presence of tinnitus and the amount of outer hair cell damage suffered. They then compared the quantity of afferent fibres between the rats that were traumatised to their unexposed, control ears. The authors reported a highly significant relationship between tinnitus and the loss of large-diameter afferent fibres throughout the cochlea. However, this loss of afferent fibres was not correlated with the amount of hearing loss present.

The authors explained that a significant loss of high spontaneous rate fibres (HSR) could decrease the amount of inhibition to the dorsal cochlear nucleus cells. Large-diameter afferent fibres are characterised by their high spontaneous rates (HSR), while small-diameter fibres mostly have low to medium spontaneous rates. HSR fibres make up the dominant source of somatic contacts to small (vertical) cells within the DCN (Liberman, 1993), and are characterised by Type II responses that provide the inhibitory input to principal DCN cells. The low to medium spontaneous rate fibres are mostly in contact with basal dendrites and somata of fusiform cells that drive the output response patterns of the DCN cells. The loss of these high spontaneous rate fibres results in hyperactivity in the dorsal cochlear nucleus, which the brain interprets as tinnitus (Bauer et al., 2007; Kaltenbach, 2000; Kaltenbach et al., 1998). However, the authors also acknowledged that the role of fusiform cells in generating tinnitus is yet to be determined because ablation of the dorsal cochlear nucleus does not eradicate the perception of tinnitus (Brozoski and Bauer, 2005).

2.4   'Non-auditory' tinnitus

The presence of tinnitus is also associated with other non-auditory conditions (somatosensory) such as temporomandibular joint disorders (Nomura et al., 2007; Wright and

Bifano, 1997) and whiplash (Levine, 1999). Tinnitus sufferers with these somatosensory conditions were reportedly able to modulate the loudness and sometimes pitch of their perceived tinnitus (Levine, 1999; Levine et al., 2003). The exact mechanisms involved are not understood, but it has been proposed that cross-modal processes are responsible. Shore (2004) explains that the cochlear nucleus receives input from both auditory and somatic pathways. Decreased auditory nerve activity (especially after deafening) disrupts both inhibitory and excitatory processes in the cochlear nucleus. This may trigger cross-modal compensatory processes from nearby cell units. Recordings of cell units in the cochlear nucleus showed increased responsiveness to somatic (trigeminal) stimulation after cochlear ablation. This has been proposed by Shore (2004) to account for the presence of somatic tinnitus.

However, the presence of somatic tinnitus may not always necessarily coincide with impaired hearing (Levine, 1999). It is therefore, unknown if the presence of tinnitus associated with such conditions are triggered by somatosensory deficits, impaired hearing or both. Thus, in this study, participants who have chronic somatosensory conditions are excluded from the main analyses. The Tinnitus Modulation Manoeuvre Checklist (TMMC) in Appendix F is used to screen for somatic tinnitus. The ability to modulate the tinnitus present by more than 20% is considered noteworthy.

2.5   Hearing Profiles: a summary of psychophysical measures of hearing

This study aims to understand the differences in cochlear function between people who have tinnitus and those without tinnitus, but who have similar hearing thresholds. A modified version of the Hearing Profiles was used in this study, which includes measures of tinnitus. The Hearing Profiles were developed at the Hearing Research Lab, University of Essex, as part of the Hearing Dummy Project (Meddis et al., 2010). They were used to model or predict the presence

of damage that can happen along the hearing pathway that results in different patterns of

hearing loss (Panda, 2010). The Hearing Profile was modified to include measures of absolute

thresholds (Chapter 5), frequency selectivity (Chapter 8 and Chapter 9), compression (Chapter

10), uncomfortable loudness levels (Chapter 11), distortion product otoacoustic emissions

(Chapter 12) and the Tinnitus Spectrum (Section 5.2 and Section 6.1).

Absolute thresholds determine the sensitivity of the whole auditory system. It is

measured using a pure tone sound and across several frequencies. Absolute threshold

measurements are non-site specific; it does not provide information on where a detectable

impairment occurs. Clinical measures of absolute threshold (audiometry) are plotted on a dB HL

scale, which is relative to average normal-hearing. Pure tone air-conduction audiometry,

together with bone-conduction audiometry is done to determine the presence of middle ear

defects. The literature to date reveals a lack of consistency between the presence of tinnitus

and absolute threshold measurements. This is because tinnitus is reported to occur in a variety

of audiometric configurations, and also in people with clinically normal-hearing (Barnea et al.,

1990; Meikle and Taylor-Walsh, 1984; Mitchell and Creedon, 1995; Pan et al., 2009).

Frequency selectivity is a measure of the influence and interference of tones at adjacent

frequencies. The ability to 'filter' out competing tones depends on good outer hair cell function.

Outer hair cell function is thought to be an active mechanism that provides extra sensitivity at

lower levels, and sharper 'tuning' of the basilar membrane (Robles and Ruggero, 2001). The

forward-masking paradigm used in this study allowed for off-frequency listening in order to

determine the frequency region that responds best to the probe frequency tested (Lecluyse et

al., 2011). There are only two known studies that investigated the relationship between

frequency selectivity and tinnitus. In Penner's (1980) study, frequency selectivity was compared

between two groups of people; those with normal-hearing (and no tinnitus), and those who

had tinnitus and hearing impairment. The measurements were made at 3000 Hz in the normal-hearing group, but at various tinnitus pitch-matched frequencies in the tinnitus group. The results suggested reduced frequency selectivity in the forward-masking thresholds in people with tinnitus. Penner (1980) hypothesised that failure of a suppression mechanism may give rise to excess spontaneous activity which is perceived as tinnitus. It is important to point out that the observations made Penner's (1980) study could also be due to the presence of hearing impairment in the tinnitus group.

Mitchell and Creedon (1995) repeated Penner's (1980) study to control for the presence of hearing impairment. They compared the amount of frequency selectivity in two groups of people with normal-hearing; one with tinnitus and the other without tinnitus. Absolute threshold measurements were similar between the two normal-hearing groups. Frequency selectivity was measured at 3000, 6000 and 8000 Hz (frequency regions where tinnitus was perceived), but differences in frequency selectivity between the two groups were only significant at 8000 Hz. The authors reported that at this frequency, the low-frequency tail end of the frequency selectivity curve in the tinnitus group was lower than the control. They suggested that this was an indication of 'hypersensitivity', which has been suggested to imply outer hair cell damage (Liberman and Dodds, 1984). There is currently no known study that investigates differences in frequency selectivity between groups of people with hearing impairment, but with or without tinnitus.

Temporal Masking Curves (TMCs) is a measure of auditory compression at the level of the basilar membrane. Compression is a consequence of nonlinear behaviour in the cochlea and results in a disproportionate increase of basilar membrane vibration with respect to signal input. This means that a signal input of 50 dB results in outputs of 10 dB in the cochlea, and in normal-hearing adults, the compression coefficient is estimated to be between 0.2 and 0.3.

(Lopez-Poveda et al., 2005). The ability to compress sounds decreases with increasing impairment and has been suggested to be caused by damage to the outer hair cells (Plack et al., 2004; Ruggero and Rich, 1991). There is no known published study that investigates the amount of compression present in people with tinnitus, using the TMC method.

Uncomfortable loudness levels (ULLs) are used as a measure of recruitment and hyperacusis, though both conditions may have separate mechanisms. The presence of recruitment has been described to be a consequence of reduced dynamic range in hearing impairment and can be due to loss of the compressive ability of the cochlea (Moore, 2007). This means that sounds become loud very quickly for a person who has recruitment. A person with normal-hearing, on the other hand, will perceive sounds to be louder at a slower rate. Hyperacusis, however, can be viewed in two ways. The first describes a hypersensitivity at the level of the auditory system (though it is unknown if it is related to recruitment). The second view involves a psychological aversion to sound, or phonophobia (Jastreboff, 2000).

Epidemiological studies suggest that hyperacusis is prevalent in at least 40% of people with tinnitus (Goldstein and Shulman, 1996). Hyperacusis is also apparent in genetic disorders such as Williams syndrome (Nigam and Samuel, 1994). However, it is not clear if these studies separate out the two suggested distinctions of hyperacusis. There are only two known studies, to date, that investigated the presence of recruitment (and used ULLs as a measurement tool) in people with tinnitus who also had hearing loss. Tyler et al. (1983b) observed that people with tinnitus had decreased sound tolerance at their tinnitus pitch, compared to regions where they did not perceive their tinnitus. Tonndorf (1981) speculated the loss of stereocilia function in his tinnitus model as an explanation for the presence of recruitment. Dix et al. (1948) compared recruitment between people with Ménière's Disease and those who had eighth nerve lesions. They suggested that recruitment was more prevalent in people who had cochlear disorders

(Ménière's Disease), and implied the use of measuring recruitment to differentiate between cochlear and retrocochlear disorders. There are no known studies that investigate the presence of recruitment in hearing impairment, but with or without tinnitus.

Comparisons between Distortion Products Otoacoustic Emissions (DPOAEs) measurements and the presence of tinnitus have only been investigated in people with normal-hearing. A number of studies have reported that DPOAE amplitudes and signal-to-noise ratios were generally lower in people who had tinnitus compared to their hearing-matched controls (Acker, 2009; Granjeiro et al., 2008; Shiomi et al., 1997). On the contrary, Sztuka et al. (2010) and Gouveris et al. (2005) both separately reported that the DPOAE amplitudes were markedly higher in groups of people with tinnitus compared to their controls, and suggested that tinnitus may be triggered by increased motility of the OHCs (due to decreased efferent activity), and not by OHC dysfunction. DPOAE responses have not been measured in hearing-impaired groups with or without tinnitus, presumably due to the higher probability of absent responses with increasing hearing impairment (Hall III, 2000).

The Tinnitus Spectrum method is used in this study as a way to quantify the perception of tinnitus. The Tinnitus Pitch-matching methods have previously been the main technique of choice to quantify the presence of tinnitus in people with tinnitus. Early studies investigated the relationship between tinnitus pitch and different associated aetiologies in the hope that the pitch match would be of diagnostic value in determining the damage that triggered tinnitus (Douek and Reid, 1968). Unfortunately, Tinnitus Pitch-matching is known to exhibit large within- and between-session variability (Henry et al., 2001; Pan et al., 2009; Penner and Saran, 1994). This is possibly because tinnitus is made up of a complex mixture of sounds with variations in sound quality (hissing, buzzing, whistling) that may change several times in a day.

A number of strategies have been developed to enable more efficient pitch matches to be made. Pitch is sometimes mistaken for loudness which may account for a percentage of variability in measurements (Moore, 2004c). Individuals are, therefore, usually trained to differentiate the between pitch and loudness before performing pitch-matching tasks. Pitch-matching has been recommended to be performed ipsilaterally to avoid problems due to binaural diplacusis (Evered and Lawrenson, 1981; Mitchell, 1983; Tyler and Conrad-Armes, 1983a). Bracketing methods were also used to find the most prominent tinnitus pitch match. A number of bracketing paradigms have been used to decrease the variability of the pitch matches. However, the lack of success with these methods reinforces the suggestion that tinnitus is a complex mixture of pitches (Henry et al., 2001; Penner and Bilger, 1989).

Noreña et al. (2002) used a rating system to characterise the tinnitus 'spectrum', to accounting for the presence of multiple pitches. Participants were firstly asked to match the loudness of a continuous pure tone to their tinnitus and then rate (on a scale of 0 to 10) how much the pitch of the tone contributed to their tinnitus. The authors observed that a relationship between the audiogram and Tinnitus Spectrum existed. Participants generally rated pure tones that fell in their impaired hearing region to have high contributions to their overall perception of tinnitus. This corroborated with results of other studies that suggested the presence of a strong relationship between tinnitus and hearing impairment (Roberts et al., 2006; Roberts et al., 2008; Sereda et al., 2011). The variability between the Tinnitus Pitch-matching task and the Tinnitus Spectrum method were compared in Section 3.4.6.

2.6   Summary

The present review on the tinnitus research has uncovered a number of caveats in the assumptions made about tinnitus. This study aims to address the limitations of previous

research and to improve the understanding of the damage that triggers the perception of tinnitus. Firstly, it is important to acknowledge that not everyone with hearing impairment has tinnitus, and it is still not fully understood why this is the case. Some authors have proposed explanations for this occurrence (Jastreboff, 1995; Kiang et al., 1970), but none of these ideas have been thoroughly investigated in people with tinnitus. In this study, therefore, comparisons were made between two hearing-impaired groups with similar hearing thresholds. This was done to uncover any possible differences in cochlear function between the two groups. A normal-hearing group acted as a secondary control group to identify the boundary between 'normal' and 'impaired'. Secondly, it is important to clearly identify the type of tinnitus (e.g. auditory versus non-auditory or permanent versus temporary perception of tinnitus) that is being studied. This is a clear disadvantage in most tinnitus studies (Savastano, 2004), because it is often not known what types of tinnitus (and associated damage that trigger the tinnitus) are being investigated. Thirdly, the use of absolute thresholds alone does not provide enough information about cochlear behaviour. In this study, therefore, a number of additional psychophysical tasks were used to estimate cochlear function (Chapter 3). These were condensed and summarised in the Hearing Profiles shown in Appendix G.

Chapter 3
Methods

This chapter provides (1) an introduction into the main design of the study, (2) detailed descriptions of the psychoacoustical measurements made and (3) justifications on the use of the Tinnitus Spectrum as the main method to quantify the perception of tinnitus. A short pilot study is described towards the end of this chapter to highlight the differences between measurements made with a Tinnitus Pitch-matching task and the Tinnitus Spectrum.

3.1   Design of the research

This study aims to understand why tinnitus is perceived in only a subpopulation of people with damaged hearing. The presence of tinnitus in this study is defined as the (1) permanent perception of phantom sound in the absence of any external stimuli that (2) is also perceived in all kinds of acoustic environment and (3) not associated with any known medical conditions such as acoustic neuroma or Ménière's Disease. Participants with tinnitus that do not meet this definition are presented as individual case studies in Appendix H and Appendix I. The original experimental design involved a quantitative method of data collection between four groups of participants:

1. Hearing-impaired participants with tinnitus

2. Hearing-impaired participants without tinnitus

3. Normal-hearing participants without tinnitus

4. Normal-hearing participants with tinnitus (Appendix H)

These four groups were originally proposed to investigate different combinations of hearing levels and presence of tinnitus. Unfortunately, there were an insufficient number of volunteers with normal-hearing and tinnitus, and this group was considered separately as case studies in Appendix H. Despite all efforts, there was an inherent difficulty to recruit participants with normal-hearing and tinnitus. One reason for this was because hearing-impaired listeners with tinnitus were sometimes unaware that they were hearing-impaired. Some volunteers who originally signed up to be in the normal-hearing group with tinnitus were not aware that they had hearing loss, and had to be relocated to the hearing-impaired with tinnitus group. Other individuals who met the criterion of normal-hearing did not have permanent tinnitus. These were excluded from the main analyses and were considered separately as case studies in Appendix H.

The main analysis focused on the comparison between two groups of people with hearing-impairment, but with or without tinnitus. The hearing-impaired groups were then contrasted against a normal-hearing and no tinnitus group, which acted as the 'normal' baseline measure. The experiments conducted include tests that were aimed at diagnosing the type of cochlear pathology that may trigger tinnitus. The following procedures were carried out in all participants:

1. Otoscopy

2. Audiometry and Tympanometry

3. Distortion Product Otoacoustic Emissions

4. Tinnitus Handicap Inventory (tinnitus participants only)

5. Tinnitus Modulation Manoeuvre Checklist (tinnitus participants only)

6. Structured Interview based on the Fonseca's questionnaire (tinnitus participants only)

7. Absolute thresholds

8. Iso-Forward-masking Curves (IFMCs)

9. Temporal Masking Curves (TMCs)

10. Uncomfortable Loudness Levels (ULLs)

11. Tinnitus Spectrum (tinnitus participants only)

3.2   Subject selection criteria and ethics

This research concerns the possibility that tinnitus is triggered by specific forms of damage to the structures in the cochlea. In order to explore this, basic screening procedures were set in place. Participants were screened for middle ear complications. Hearing-related medical histories of participants were obtained, together with a full description of their tinnitus. A structured interview pertaining to jaw problems was also conducted to uncover temporomandibular conditions that could be associated with the perception of tinnitus.

Participants were recruited from (1) National Health Service tinnitus clinics in the Colchester and surrounding areas, (2) staff and student members of the university, (3) relatives of staff and student members of the university, (4) advertisements placed in the university's monthly magazine, (5) advertisements placed in the Action on Hearing Loss' (formerly Royal National Institute for Deaf People) quarterly magazine and (6) advertisements placed in the Hearing Care Centre's (private hearing-aid clinic in Colchester) quarterly magazine. Volunteers were recruited on the basis that they were interested in the project and *no* attempt was made to screen for specific types of hearing impairment, such as noise-induced hearing loss. In fact, participants with self-reported noise trauma were present in both hearing-impaired groups. About two-thirds of the hearing-impaired participants responded from advertisements made at the university.

Informed consent was obtained from all subjects in accordance with the procedures approved by the Essex1 Research Ethics Committee (REC reference number: 08/H0301/134) and by the ethics committee at the Department of Psychology, University of Essex. All participants were allocated identity codes to preserve anonymity. They were also informed that their participation was voluntary and that they could withdraw at any point, without detriment to their medical or legal rights. The documents associated with the recruitment process are appended at the end of the thesis.

All volunteers were not paid for their participation, but any travel expenses to and from the university were reimbursed. Participants were advised to attend a series of 5 sessions, each lasting about 2 hours. This was a generous estimate of the total amount of time required to obtain a full hearing profile, which also included additional practice and repeat measurements. Frequent breaks were also allocated in the time frame (about 10 minutes break every half an hour). The total number of participants is as shown below:

Table 3.1: Participants recruited.

	No Tinnitus, Hearing-Impaired N = 15 (6 ♀)	Tinnitus, Hearing-Impaired N = 27 (8 ♀)	Normal-hearing, no Tinnitus N = 19 (8 ♀)
Mean Age	64	59	32
Std. Dev.	15	10	9

Eight other participants (mean age 52 ± 1 SD = 7 years, 5 females) had non-permanent tinnitus or other aetiologies that could have triggered their tinnitus. This group also included people who had normal-hearing and permanent tinnitus (N = 2), because the number of participants in this group were too small to be regarded in the main analyses. These eight participants were not included in the main analyses and referred to in Appendix H and Appendix I.

3.3   Screening and basic clinical testing

Otoscopy

Otoscopy was performed according to the procedures outlined by the British Society of Audiology (Audiology, 1992). This was done to inspect the fidelity of the ear canal and the tympanic membrane. Participants with suspected outer and middle ear conditions that may give rise to tinnitus were excluded from the study. These included the presence of impacted wax, perforated tympanic membrane or middle ear pathologies.

Audiometry and Tympanometry

Air- and bone-conduction audiometry were both measured using a calibrated Kamplex A222 Clinical Audiometer and Tympanometer with a pair of supplied TDH39 headphones and a standard B71 bone conductor. Measurements were made between 250 Hz to 8000 Hz. The machine was used to record the ear canal volume, peak pressure and peak compliance of the participants. These were used to ensure that the participants' middle ear functions were within the normal limits as indicated by recommended British Society of Audiology procedures (Audiology, 1992). Participants with suspected middle ear abnormalities were excluded from the study and advised to see their General Practitioner for medical attention.

Distortion Products Otoacoustic Emissions (DPOAEs)

DPOAEs were measured with the Otodynamics Echoport ILO292-II system. Measurements were made using two stimuli, at frequencies f_1 and f_2 and at levels L_1 and L_2. Distorted acoustic elements generated in the cochlea were recorded by a microphone at the ear canal. These distorted products had a frequency at f_{dp} where $f_{dp} = 2f_1 - f_2$. DPOAEs were measured in all participants at the recommended screening ratio of 1.22 and with L_1/L_2 set at

65/55 dB SPL. The criteria to identify the presence of DPOAE was set according to Barker et al. (2000)'s study, where the signal-to-noise ratio is more than or equal to 6 dB, with a distortion product response magnitude exceeding -5 dB SPL.

DPOAE measurements were preceded by checks to ensure normal outer and middle ear function. A DPOAE probe is then placed at the entrance of the ear canal and the Otodynamics check fit test performed. The check fit biphasic click stimulus was used to correct for differences in ear canal size. The fit of the probe is estimated by visually inspecting for anomalies in the frequency response. In general, a biphasic shape without excessive 'ringing' and with a smooth distribution across the stimulus spectrum is acceptable.

Although the levels of the DPOAE stimuli were set at 65/55 dB SPL, the actual levels can vary. This discrepancy exists because the probe is not always at the same distance or angle from the tympanic membrane. All DPOAE recordings were performed until the default number of sweeps was reached (260 sweeps). Participants were advised to keep jaw movements to a minimum and to remain comfortably still for the duration of the measurement. Recordings were repeated in cases where excessive amounts of external noise were present, due to sudden jaw movements (coughing).

Tinnitus Handicap Inventory (THI)

The Tinnitus Handicap Inventory is a questionnaire that was developed to evaluate the impact of the severity of tinnitus on an individual (Newman et al., 1996). The participant had to answer 'yes', 'no' or 'sometimes' to a set of questions. The scores were weighted with 'yes' given a score of 4, 'sometimes', a score of 2 and 'no', a score of 0. The participant had to answer all of the questions presented. The scores were added up and the final score was interpreted with different gradations of severity, for instance, total scores up to 16 were interpreted as

slight tinnitus (only heard in quiet environments), scores between 18 to 36 were interpreted as mild (easily masked by environmental sounds and easily forgotten with activities), and so on. The THI questions and scoring sheet are in Appendix D.

Structured Interview

The basis of the structured interview was similar to that presented in the Fonseca questionnaire (Nomura et al., 2007), and was conducted to uncover suspected temporomandibular joint disorders. It was important to make note of any such disorders because they have been associated with the presence of tinnitus. Although it is not known for sure if such disorders are responsible for triggering tinnitus, they have been reported to co-exist with the condition (Wright and Bifano, 1997). The structured interview form is in Appendix E.

Tinnitus Modulation Manoeuvre Checklist (TMMC)

The TMMC was used to assess the amount of influence the somatosensory system had on the perception of tinnitus. Participants were asked to perform a number of head and neck movements and to report the change (if any) in the perception of their tinnitus. These specific movements inspect the influence of known cranial nerves on the perception of tinnitus. For instance, cranial nerves 1 and 2 correspond with neck flexion and movement, cranial nerves 3, 4 and 6 correspond with eye movements, cranial nerve 5 with the jaw, cranial nerve 7 with facial expression, cranial nerve 11 with shoulder movement and cranial nerve 12 with tongue movement (Simmons et al., 2008). This information is particularly useful when examining the case studies in Appendix I. The TMMC questionnaire is in Appendix F.

3.4   Psychoacoustic testing

All psychoacoustical tests were conducted in a double-walled sound treated room using a pair of Sennheiser HD600 headphones. An M-Audio Audiophile 2496 36-bit sound card was used on a DELL computer with Intel 2 Duo 3 GHz processor with 3.25GB RAM, with a Windows XP operating system. The MultiThreshold 1.39 software program ran on the MATLAB R2007a platform. Pure tone sinusoids were used as both masker and probe tones throughout the psychophysical tasks. Participants sat in front of a computer screen that displayed a graphical user interface with an image of the response pad. A Cedrus RB-834 response pad was placed on the table in front of the participants, which matched the buttons on the computer screen in front of them (Figure 3.1).

(A) Computer Screen   (B) Cedrus response pad
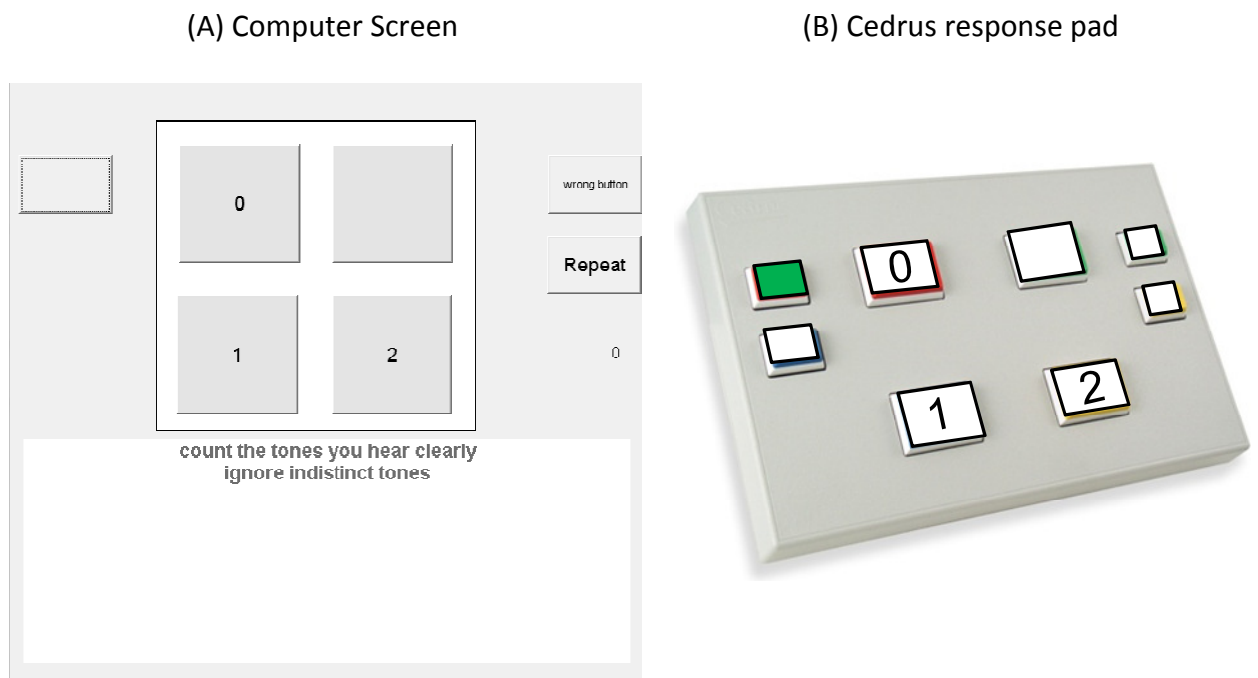
Figure 3.1: (A) Screenshot of the graphical user interface on the computer screen and (B) the Cedrus response pad used in the study.

The participants were instructed to press the green 'GO' button at the start of the trial and to count the number of 'beeps' (tones with longer duration) or 'clicks' (tones with shorter duration) heard. They were also informed about the 'Repeat' button that could be used if they happened to cough or sneeze when the sounds were presented, but they were advised not to use it too often as it would slow down the testing time. In all of the psychoacoustical tasks, the participants were instructed to count only the tones that they were certain of and to ignore the ones that they were unsure of.

The buttons on the screen disappeared when the stimuli were presented and the participants had to make their choice after the buttons reappeared on the monitor. Participants were also advised to stop the tests midway and to inform the experimenter if the sounds presented were too uncomfortable. Participants who took too long to decide whether or not they heard the tones were reinstructed, and reminded that it was a simple binary task, and all that was required was a simple 'yes, I heard it' or 'no, I did not hear it' decision making process.

The use of catch trials was an important part of the single-interval up-down method used in all of the tasks (Lecluyse and Meddis, 2009). The program included random presentations of 'no tone' trials in order to check that the task was done correctly. During these presentations, if the participants counted a tone during a catch trial, the graphical user interface will turn red and an error sound would be played through the headphones. The participant is then instructed to resume testing by pressing the green 'GO' button to begin again.

In general, if the participant made more than 5 catch trial errors, the task was aborted they were allowed a short break to recuperate. They were also reinstructed by informing them that the error on the screen indicated that they counted an absent tone. In rare cases, if the participants pressed the buttons on the respond pad too quickly (before the buttons appeared

on the monitor screen) the program would take in the current response as the next one. This meant that if the following trial was a catch trial, and they counted '2' on the previous trial, an error would appear. The participant would then be reminded to wait for the buttons to reappear on the screen before pressing the buttons on the response pad.

The single-interval up-down paradigm differs from traditional 2-alternative forced-choice methods, because it makes use of cues to allow easier usage. The method generally consists of two sets of stimuli. The first set acts as a *cue*, and is set at an audible level to help the participants attend to the task. The second set comprises of the *test* stimuli. Participants count '1' ('no' response) if they only hear the *cue*, and '2' ('yes' response) if they hear both the *cue* and *test* stimuli. In some instances, they may not be able to hear the cue, probably due to lapse of attention; '0' ('no' response) is selected in such cases.

The procedures used were the same as those outlined by Lecluyse and Meddis (2009). The initial step size of the adaptive procedure was set at 10 dB. The initial threshold is gradually reduced until the first 'no' response is encountered. The stimulus level is then set to the mid-point between the previous two levels, and a smaller step size (2 dB) is used instead. The adaptive procedure continues until a fixed number of runs (10 runs) from the start of the first 'no' response has been reached. The program also checks for the presence of reversals, and if none is encountered within a set number of runs (80% of the fixed number of runs), the program resets the number of runs.

Participants were informed to be very conservative with their responses and to count only the stimuli that were confidently heard. The conservative judgement approach acted as a baseline guide in defining the listener's criterion on the task, and helped minimise the 'guessing rate' of responses. Lecluyse and Meddis (2009) did not find any differences between their method and the 2-alternative forced-choice task. The main benefit of the single-interval up-

down method is the speed and ease of the task to administer, whilst achieving an acceptable

level of accuracy.

3.4.1 Absolute Thresholds

(A) Schematic of stimuli used in absolute
threshold task
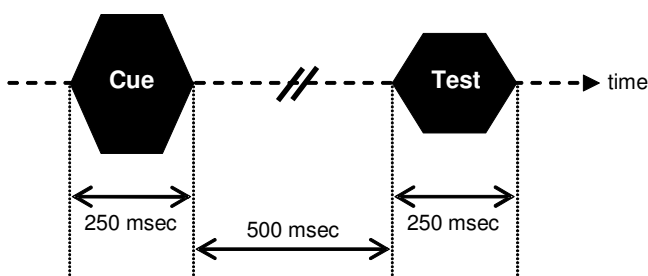
(B) Absolute threshold
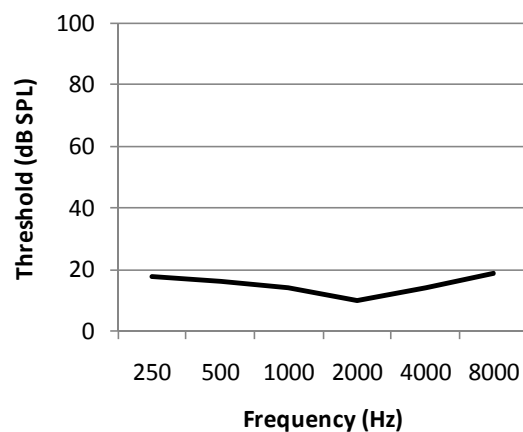
Figure 3.2: (A) Schematic of the pure tones presented in the absolute threshold method. (B) An example of normal-hearing absolute threshold.

Pure tone sinusoidal signals were used to measure absolute thresholds. The

measurement method used was the cued single-interval up-down paradigm described by

Lecluyse and Meddis (2009). The cue and test tones were separated by 500 msec. Both signals

were ramped with raised cosine onset and offset times of 4 msec. Signal durations of 250 msec

and 16 msec were used in the measurements. The schematic representation of the cue and the

test tone is shown in Figure 3.2.

In this task, participants were told that they would be tested using two different types

of tones (across separate trials), and across different frequencies. The first set of tones sounded

like a long 'beep' and the other set was a much shorter 'click'. The participants had to count the

number of 'beeps' *or* 'clicks' heard in the task. In general, all the participants tested could

perform this task with little effort. The verbal instructions given to participants were as follows,

"The aim of this task is to find out what's the quietest sound you can hear at different

frequencies, using two sets of sounds. The first set sounds like 'beep beep' and the second set

sounds more like 'click click'. Your job is to count only the ones that you're *absolutely* sure of.

There may be times when you are not sure if you've heard the second beep or click, but if you

think you may be guessing or if you are unsure, then don't count it. Count *only* the ones that

you are *absolutely*, *positively* sure of."

3.4.2   Iso-Forward-masking Contours (IFMCs)

(A) Schematic of stimuli used in Iso-Forward-masking task
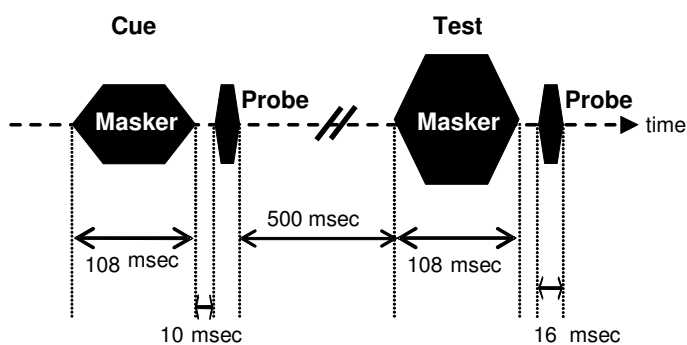
(B) Iso-Forward-masking contours
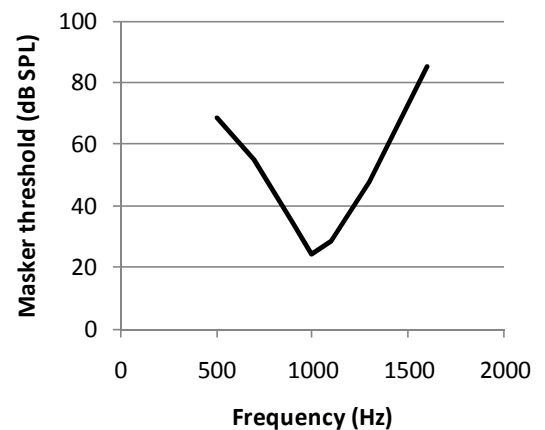
Figure 3.3: (A) Schematic of the forward-masking stimuli used to obtain the Iso-Forward-masking Contours (IFMCs). (B) An example of a normal-hearing IFMC.

Frequency selectivity can be estimated with the use of psychophysical tuning curves

(PTCs). PTCs are conventionally measured using simultaneous-masking with notched noise

maskers. In this study, however, a forward-masking paradigm is used instead (Figure 3.3). The

forward-masking paradigm is preferred because it eliminates the occurrence of beats, which may be apparent in simultaneous-masking paradigms. Notched-noise is used in some PTC measurements to remove the influence adjacent frequencies would have on the probe tone, as would be the case in off-frequency listening. However, in this study, the presence of these off-frequency shifts is of interest and will be investigated in detail. In order to avoid confusion and comparison, the term 'PTCs' will not be used in this study. The term Iso-Forward-masking Contours (IFMCs) will be used instead. An IFMC is defined in here as the function obtained when connecting masker levels that just mask the levels of the test probe.

The maskers and probes were both sinusoids, with masker duration of 108 msec, probe duration of 16 msec, and a masker-probe gap of 10 msec (Figure 3.3). IFMCs were measured with the level of the test probe set at 10 dB Sensation Level (SL), and at masker frequencies with ratios of 0.5, 0.7, 0.9, 1, 1.1, 1.3 and 1.6 to the probe frequency, F_p. The masker level was set at a start-up value that was 20 dB SPL lower than the probe level. IFMCs were measured across at least 5 frequencies between 250 Hz to 8000 Hz. Absolute threshold measurements were always performed twice before measuring the IFMCs to set the level of the test probe.

Participants were informed that the maskers were called 'beeps' and the probe tones were called 'clicks'. The participants were informed that testing would begin by counting just the 'clicks' only (absolute threshold measurement). The IFMC task was performed after the absolute threshold measurement. In the IFMC task, participants were told that they will be able to hear the 'clicks' at the start of the task (the probe level was set at 10 dB SL). The participants were then informed that they would start hearing 'beeps' that would gradually get louder and louder to try and make it difficult for them to hear the 'clicks'. They were told to count only the 'clicks' and to ignore the 'beeps'. For example, the sequence 'beep-click, beep-click' (for two

clicks), or the sequence 'beep-click, beep' (for one click) could be heard. They were also told that the 'clicks' always occurred at the tail end of the 'beep'.

Participants were told the task would be a little 'tricky' for some of the frequencies tested, but were encouraged to try their best. In most instances, the participants did not require further training after the instructions. It was possible to check if the IFMC task was done properly by ensuring that the level of the masking threshold at the probe frequency, F_p obtained, was above the absolute threshold value at that frequency. Participants who found the IFMC task difficult were provided with extra practice.

Practice was initiated by starting the first IFMC trial with a masker frequency ratio of 0.5 or 0.7 from the probe frequency, so that it was easier for the participant to tell the difference between the 'beep' and the 'click'. Another option was to set the start of the masker level at 40 dB SPL below the probe level, so that the participant would be able to acclimatise to listening to just the 'clicks' for a longer period of time. It was sometimes required to be in the testing room with the participants to reassure them during practice and to check that they could identify the 'clicks' in isolation and to determine that they knew when they were presented with the 'beeps'.

The verbal instructions given to participants were as follows, "We will start this task by measuring just the clicks first so you know what they sound like. Then we will start the next task. In this task, you will hear the clicks again. This time they will be very quiet, but they should be there. After a while, you will hear beeps that will gradually get louder and louder to try and make it difficult for you to hear the clicks. Your job is to count only these clicks, and ignore the beeps. So, sometimes, you may hear 'beep-click, beep-click' for two clicks, or other times, you may hear 'beep-click, beep' for only one click. It may be difficult sometimes to hear these clicks,

but try your best and don't forget to count *only* the *clicks* that you're *absolutely, positively* sure of."

3.4.3 Temporal Masking Curves (TMCs)

(A) Schematic of stimuli used in Temporal
Masking Curve task
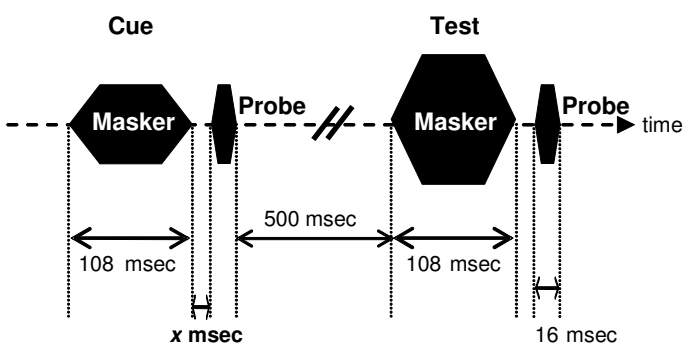
(B) Temporal Masking curve
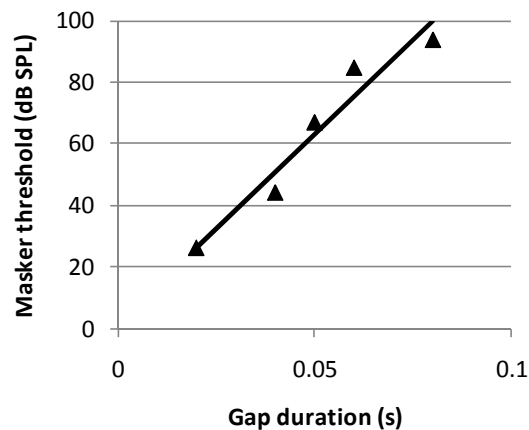
Figure 3.4: (A) Schematic representation of the Temporal Masking Curve (TMC) stimuli used. (B) An example of a normal-hearing TMC.

The Temporal Masking Curves (TMC) method was used in other studies as a measure of compression in order to estimate the input/ output function of the basilar membrane (Lopez-Poveda et al., 2005; Nelson et al., 2001). The input/ output function requires a set of at least 10 TMC measurement points to be modelled. The TMCs are used in this study, however, as a relative indicator for the amount of compression present. A reconstruction of the input/ output function is not required in this study. A set of 5 measurement points was, therefore, sufficient to estimate the relative amount of compression.

The TMCs carried out in this study used the same forward-masking method as the IFMCs, but with the exception that the gap duration between the masker and the probe was

varied by *x* msec (Figure 3.4). Measurements with gap durations of 20, 40, 50, 60 and 80 msec were measured at the same frequencies as the IFMCs. Absolute threshold measurements were also made twice before starting the TMC task, and the level of the probe was set at 10 dB SL.

The TMC task was performed after participants were confident with the IFMC task. The participants were informed that the TMC task was similar to the IFMC task except that the gap between the 'beep' and the 'click' could change. Again, the sequence of the sounds that would be heard was explained, for instance, 'beep-----click, beep------click' (for two clicks), or 'beep-click, beep-click' (again for two clicks) for when the gap between the masker and the probe was shorter.

The verbal instructions given to participants were as follows, "This task is similar to the previous one with the beeps and clicks (IFMCs), but with a slight difference. In this task, the gap between the beep and the click can change, so sometimes, it sounds like 'beep-----click, beep-----click' for two clicks, and other times, it's 'beep-click, beep-click' for two clicks again. You have to do the exact same thing as you did before - count *only* the *clicks* that you are *absolutely positively* sure of."

3.4.4   Uncomfortable Loudness Levels (ULLs)

Uncomfortable Loudness Levels (ULLs) are measures of loudness discomfort that are generally used in audiological assessments. In this task, participants were asked to indicate the maximum level of tolerance to a single pure tone that was 500 msec long, measured at 250, 500, 1000, 2000, 4000, 6000 and 8000 Hz, and in increments of 5 dB SPL. ULLs in this study are used as a measure of recruitment, which is linked to loss of outer hair cell function. When the nonlinear function is impaired, the perception of loudness grows linearly, which causes sounds that are normally tolerable to be perceived louder than it is (Moore, 2007).

The verbal instructions given to participants were as follows, "You will hear a long beep in this task, and you have to decide if it is comfortable (button '0'), loud (button ('1') or uncomfortable (button '2'). The sound will gradually increase in loudness after each time you press the button. Press the 'uncomfortable' button when you think that the next sound will be too loud or painful to you. The program will stop and not play sounds to you at this level. This means we will never reach the levels at which sounds may be painful to you."

3.4.5 Quantifying Tinnitus

In this section, two methods of quantifying the perceptual properties of tinnitus will be described. These are the Tinnitus Pitch-matching task and the Tinnitus Spectrum method. The methods do not enforce the assumption of the presence of a predominant pitch, since the perception of tinnitus may consist of a variety of different pitches (Noreña et al., 2002; Pan et al., 2009; Roberts et al., 2006; Roberts et al., 2008; Sereda et al., 2011). Both methods of quantifying tinnitus in this study allow for the possibility that tinnitus is a complex mixture of pitches. The methods were programmed in MATLAB by the author. The main output of the program was a startup screen that allowed adjustments of the parameters used in the program. The signals have 4 msec cosine ramps and a sample rate of 44.1 kHz. The maximum output of the program was set at 110 dB SPL as a safety feature, and also to eliminate the possibility of signal clipping and the occurrence of distorted outputs. The duration of the signals for both tasks were set at 2 seconds, and the frequency range tested was between 250 to 8000 Hz. The initial frequency was selected randomly before the start of the procedure.

A novel approach was also introduced whereby the absolute thresholds could be entered into the program before the test began. This meant that subsequent adjustments to either loudness or pitch of the tones could be made in terms of sensation level (relative to

absolute thresholds). This was thought to be advantageous, as it would take less time to complete the task. The consequences of implementing this system will be discussed in later sections.

An important point to make was that neither the Tinnitus Spectrum method nor the Tinnitus Pitch-matching method, carried out in this study, attempted to 'guide' the listener to a fixed frequency range when making pitch judgements. This differs from most other studies that implement a bracketing technique that attempts to guide the listener to identify the most prominent pitch heard in their tinnitus (Henry et al., 2004a; Henry et al., 2000). Bracketing techniques are based on 2-alternate forced-choice adaptive methods. The method firstly locates the maximum and minimum frequency range within which the tinnitus was heard. Movements to newer frequencies are then further bracketed in smaller step sizes (between the maximum and minimum frequencies) until a single frequency value is obtained. Octave confusion is subsequently checked by presenting the participant with frequencies that are one octave above and another one below the final pitch match. Octave confusion relates to judgement errors in the perception of pitches that are an octave apart from each other, and is present even in normal-hearing listeners. The presence of octave confusion is more apparent for tones above 5000 Hz that do not evoke a clear sense of melody (Moore, 2004b).

The first method used in this study was a Tinnitus Pitch-matching task, which required participants to match a pure tone sinusoid to their perceived tinnitus. Adjustments of pitch and loudness could be freely made without any attempt to guide the participant in making pitch judgements, as would be the case with a bracketing technique. The Graphical User Interface (GUI) used in this task is shown in Figure 3.5. Firstly, participants were instructed to match the loudness of a pure tone to their tinnitus, followed by pitch adjustments. A novel approach was introduced to perform subsequent pitch adjustments (following the first one made), in

sensation level. This was achieved by entering the participant's absolute thresholds into the program before the start of the task.

Loudness adjustments could be made in step sizes of 2 dB SPL ('louder'/ 'quieter' buttons) or 5 dB SPL ('much louder'/ 'much quieter'). Similarly, pitch adjustments could be made in 0.25 octave steps ('lower'/ 'higher') or 0.5 octave steps ('much lower'/ 'much higher'). Participants could freely readjust the loudness of the pure tones after pitch adjustments if they felt that the pure tones were louder (or quieter) than their tinnitus. In such cases, the participants were reminded that loudness adjustments should always precede pitch judgements. The program offered the option of playing back the pure tones ('Repeat') or making it last for a longer duration of 5 seconds ('Loop'). The 'Done' button would be selected when participants were happy with the match and would like to end the program. The pitch-matching task was repeated at least 3 times to estimate the frequency range of the participant's perceived tinnitus.

(A) Loudness adjustments

(B) Pitch adjustments
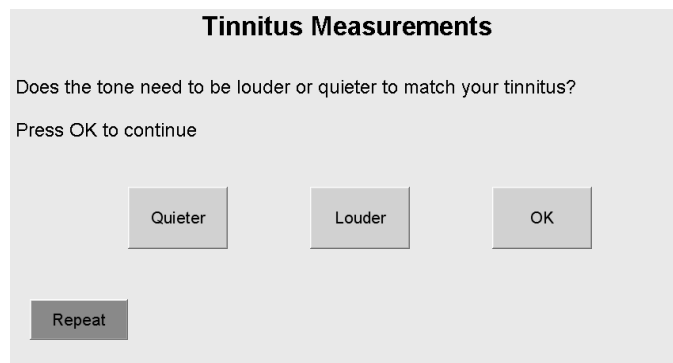
Figure 3.5: The loudness of the pure tone is first adjusted in (A), followed by pitch adjustments that can be done in (B).

The verbal instructions provided to participants were as follows, "The aim of this task is to find out what your tinnitus sound like. The first thing you have to do in this task is to adjust the loudness of the sound to match your tinnitus. Once you are happy with the loudness, click on the next button. On this page, you can adjust the pitch of the sound to match your tinnitus. On both pages the top two buttons help you make adjustments in smaller steps and the bottom two buttons (Much Quieter/ Louder/ Higher/ Lower) help you make adjustments in bigger steps. The loop button plays it back for about 5 seconds (instead of 2 seconds) and you can also use the 'Repeat' button if you have to. If you are happy with the pitch of the tinnitus, click on 'Done' and the program will end."

The Tinnitus Spectrum method was the second technique used to quantify the perception of tinnitus in this section. The MATLAB program written to obtain the Tinnitus Spectrum method was based on Noreña et al.'s (2002) study (see Figure 3.6 for the screen shot of the graphical user interface). In this task, participants were first asked to adjust the loudness of a pure tone to match their tinnitus. Next, they were asked to rate (on a scale of 0 to 10) how similar the pure tone was to their tinnitus (see Figure 3.6B). This series of instructions were repeated for a random set of 21 frequencies between 250 to 8000 Hz, which were spaced 0.25 octaves apart. A 'Repeat' button could be used to play the tone back again.

The Tinnitus Spectrum method in this study was modified from the original method to make adjustments in sensation level. This meant that subsequent pure tones presented to the listener, after the first one, would start at the same sensation level. Participants had the option of adjusting the loudness of the pure tone to that of their tinnitus before rating the pitch, and were familiarised with the range of frequencies tested before starting the task.

(A) Loudness adjustments
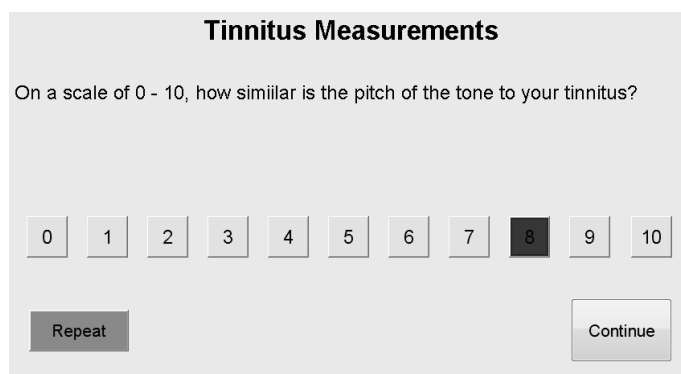
Tinnitus Measurements

Does the tone need to be louder or quieter to match your tinnitus?

Press OK to continue

| Quieter | Louder | OK |

Repeat

(B) Pitch rating

Tinnitus Measurements

On a scale of 0 - 10, how simiilar is the pitch of the tone to your tinnitus?

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

Repeat   Continue

Figure 3.6: Graphical user interface of screen seen by participants. The (A) loudness of the pure tone was adjusted first, followed by (B) the pitch rating.

The verbal instructions given to participants were, "The aim of this task is to find out how similar the pitches of these sounds are to your tinnitus. The first thing you have to do in this task is to adjust the loudness of the sound to match your tinnitus. When you are happy that it's about the same loudness, press OK. You will then be asked to decide, on a scale of 0-10, how similar the pitch of the sound is to your tinnitus. '0' means that the pitch is completely wrong and '10' means that it is a perfect match. Try and use the full scale provided. Once you decide on a number, click on the corresponding button. If you make a mistake, you can change your choice by clicking on a different number. Once you are happy with your choice, click 'Continue' and the program will move on to the next tone. You have to repeat the same thing

over a set of 21 different tones. The tones are about 2 seconds long, and you can use the 'Repeat' button to play the tone back again if you have to."

3.4.6   Pilot Study: Preferred method to quantify tinnitus pitch

The following pilot study was carried out to investigate which of the two methods, described in the previous section, would be better at quantifying the perceptual qualities of tinnitus. The amount of variation generated by the two methods will be compared. Tinnitus Pitch-matching tasks have always been reported to have large within-subject variation (Henry et al., 2004b; Penner and Saran, 1994; Tyler and Conrad-Armes, 1983a). The large variation has been attributed to the clinically reported subjective perception of tinnitus itself, and the difficulty of matching the *quality* of the tinnitus heard to either pure tone sounds or narrowband noise. The loudness and pitch percept of tinnitus have also been reported to vary at different times of the day and aggravated by emotion or stress. Most pitch-matching tasks are designed to use variations of the bracketing method to find the most prominent pitch (Henry et al., 2001). This could be another source of variability if a prominent pitch does not exist. Bracketing methods are designed to find a single pitch value and do not account for the presence of multiple pitches or the different sound qualities of tinnitus.

The Tinnitus Spectrum method was devised by Noreña et al. (2002) to study the 'internal tinnitus spectra' that represents the contribution of different pitches to the percept of tinnitus. This method utilises a 0 to 10 rating system for each pitch. A '0' rating meant that the pitch did not contribute at all to the tinnitus, while a '10' rating meant that the pitch of the tone contributed a lot to the percept of tinnitus. The method allowed for the possibility of multiple pitches to be present and does not restrict the user to concentrate on a prominent pitch. The authors reported satisfactory repeatability in their method that was only tested on hearing-

impaired individuals with tinnitus. The main observation made by the authors in Noreña et al.'s (2002) study was that the Tinnitus Spectrum method mirrored the absolute threshold results. Pure tones at frequencies that were rated to be very similar to the percept of tinnitus coincided with frequencies that had raised thresholds. The Tinnitus Spectrum was also observed to plateau at frequencies with raised thresholds. Noreña et al. (2002) suggested that the plateau represented the combination of pitches that would contribute to the variations of sounds heard by tinnitus sufferers. However, the Tinnitus Spectrum method has only been investigated in hearing-impaired individuals with tinnitus. The fundamental use of the Tinnitus Spectrum to identify pitch, compared with other tinnitus matching methods, or if the method is more susceptible to octave confusion has yet to be thoroughly investigated.

The Tinnitus Pitch-matching method carried out in this study, allows the participant full control over the loudness and pitch of the matching tone. The method differs from other studies because (1) it does not restrict the listener to a smaller set of frequencies from which the Tinnitus Pitch-matching task can be carried out and (2) it does not assume the presence of a predominant pitch in the perception of tinnitus.

The following pilot study compares the Tinnitus Spectrum method with the Tinnitus Pitch-matching method in identifying pitch at three different frequencies (500, 2000 and 4000 Hz) in individuals with normal-hearing. Adaptive bracketing techniques were not implemented in this study. This was deliberately done because the assumption of the presence of a prominent pitch is not enforced in either of the two methods of quantifying tinnitus.

Methods

18 participants with normal-hearing were tested in this pilot study. They were assessed to have normal outer and middle ear function by performing otoscopy and tympanometry.

Absolute threshold measurements were obtained at 250, 500, 1000, 2000, 3000, 4000, 6000

and 8000 Hz. Participants had normal-hearing if their absolute threshold measurements did not

exceed 20 dB SPL higher than the reference sound pressure level (RETSPL) for circumaural

headphones (BSI, 2004). Three frequency groups were tested (500, 2000 and 4000 Hz). Each

participant was allocated to one of the frequency groups.

Tinnitus was simulated ('*pseudo tinnitus*') in the contralateral ear with a 40 dB SL pure

tone, at the test frequency. Participants were required to listen to this '*pseudo* tinnitus' for a

duration of 60 seconds before the start of the task to control for loudness adaptation (Hellman

et al., 1997). Feedback from initial tests suggested that pseudo tinnitus stimulations at 20 dB SL,

although closer to the reported loudness of tinnitus (Henry and Meikle, 2000), were almost non

perceivable after a period of time. This corroborated with Hellman et al.'s (1997) report of a

50% decline in loudness perception for continuous tones of 20 dB SL. Pure tones of 40 dB SL

were therefore used to account for this effect. Participants were tested in random sequence

with the two methods and were familiarised with the range of frequencies tested before

starting the task.

Results

The results of both methods were averaged over 3 runs and across the 6 participants in

each group (Figure 3.7). The average of the maximum values on the Tinnitus Spectrum was

used as an indication of the pitch of the pseudo tinnitus presented. This was based on Noreña

et al.'s (2002) observation of a *plateau effect* of the Tinnitus Spectrum in hearing-impaired

sufferers. The plateau in Noreña et al.'s (2002) study, mirrored the region where hearing-

impairment was present and the frequencies in this plateau was suggested to contribute

significantly to the percept of tinnitus. In this pilot study, however, the pseudo tinnitus was

simulated by a single pure tone. Therefore, the maximum rating on the Tinnitus Spectrum would be regarded to have the most significant contribution to the pseudo tinnitus heard.

Correlation analyses suggest a significant relationship between the Tinnitus Spectrum method and the pseudo tinnitus (r = 0.84, p = 0.00004). Also, between the Tinnitus Pitch-matching task and the pseudo tinnitus (r = 0.70, p = 0.001). The variability between the two methods were not found to be significantly different (t(18) = -1.36, p = 0.904), although the Tinnitus Spectrum performed better than the Tinnitus Pitch-matching task at low frequencies.
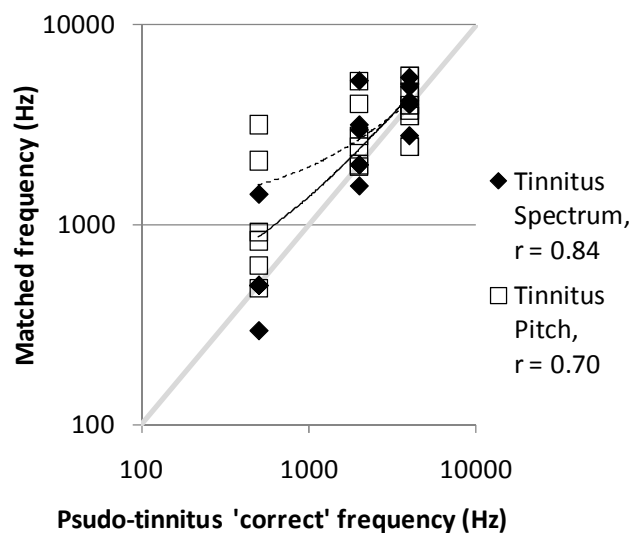
Figure 3.7: Frequency matches measured using the Tinnitus Spectrum method (filled diamonds, solid line) and the Tinnitus Pitch-matching method (open squares, dotted line), tested at 500, 2000 and 4000 Hz.

Discussion

The results suggested that on average, the peak (maximum) value on the Tinnitus Spectrum (TS) was a better predictor of the pseudo tinnitus than the Tinnitus Pitch-matching method used in this pilot study. The observations made in this pilot study are explained by a number of different factors. Firstly, the two methods may require different amounts of training in order to be completed successfully. In this study, only a minimal amount of training was

given to both groups. This was done deliberately as most people tested in the main tinnitus study would be naive listeners and it would not be possible to allow for extensive practice sessions due to time constraints. Although participants were familiarised with the range of frequencies used before performing the Tinnitus Pitch-matching method, they were not obliged to listen to the full pitch range when carrying out the task itself. Some participants could, therefore, have made judgements relative to the previous pitch heard, rather than making comparisons to the pseudo tinnitus. For instance, if the pseudo tinnitus was at 2000 Hz, and the current matched pure tone was at 6000 Hz, the participant could decide that the 6000 Hz was much higher in pitch than the pseudo tinnitus, and choose to decrease it slightly by two step sizes. If smaller step sizes were used, the matching tone would be at about 4000 Hz, and the participant, accepting that this is now a closer match to the pseudo tinnitus, might decide to accept this as a close match and end the experiment prematurely.

Secondly, octave confusion was also more apparent in the Tinnitus Pitch-matching method compared to the Tinnitus Spectrum task. Octave confusion testing was not enforced in this pilot study, so no conclusions can be drawn as to which method would be more susceptible to octave confusion. The large variation in the tinnitus pitch-match task has been reported in earlier Tinnitus Pitch-matching studies (Burns, 1984; Tyler and Conrad-Armes, 1983a). In the Tinnitus Spectrum task, however, the presence of mild plateaus close to the maximum rating on the Tinnitus Spectrum may be evidence of octave confusion. However, this can be accounted for by analysing only the maximum rating on the Tinnitus Spectrum.

Thirdly, the increase in accuracy of the Tinnitus Pitch-matching task at matching tones at higher frequencies suggested that the ability to pitch-match is easier at higher frequencies. However, this is not the case. The ability to discriminate between pitches degrades with increasing frequency (especially beyond 5000 Hz), because pitches in this region do not evoke a

clear sense of melody (Moore, 2004b). This has been shown to be the case regardless of the duration of tones used (Skinner, 1970; Skinner and Antinoro, 1968, 1969). The other possible explanation for the low-frequency match for the Tinnitus Pitch-matching task may be influenced by the random start value. On average, the random starting values for the 500 Hz tone was at about 2300 Hz (+2 octaves), 2000Hz was at about 1500 Hz (-1/2 octave) and the start value for 4000 Hz was at about 2700 Hz (-2 octaves). It would seem that making pitch judgements from a descending order (from high to low frequencies) may evoke more errors than making pitch judgements from an ascending order (from low to high frequencies). This may be an important observation when conducting future pitch-matching studies. Indeed, some participants reported that it 'felt' easer to perform the task if they gradually increased the pitch of the matching tone, to the *pseudo tinnitus*. However, difficulties may arise when implementing this strategy on people with tinnitus because (1) the precise location of their pitch is often unknown, and (2) the tinnitus heard may often be comprised of a complex combination of both low- and high-pitched tones. Additional strategies may need to be set in place to overcome this.

Fourthly, the novel method introduced in this task may have also been another cause for concern in the Tinnitus Pitch-matching task. It was anticipated that making pitch adjustments in sensation level would (1) reduce the amount of time taken to complete the task, and (2) make the task simpler for participants as they would not have to make lengthy loudness readjustments. However, it was noted that some participants, did in fact, have to make more loudness readjustments. This was due to the presence of irregularities in absolute threshold measurements; the measurements made at regular intervals do not always guarantee a smooth function. One way of overcoming this would be to make absolute threshold measurements every 0.25 octave instead of every 1 octave. However, this would mean at least doubling the

amount of time required to complete the task. The Tinnitus Spectrum was not affected by this

additional method as participants only made loudness adjustments *once* before deciding on

pitch ratings.

The rating system implemented in the Tinnitus Spectrum method could also be

important in identifying pitch. The freedom to decide on a rating, rather than manual pitch

manipulations may be essential to better pitch identification. This was demonstrated by studies

done by Pan et al. (2009) and Moore et al. (2010) (see Table 3.2).

Table 3.2: Tinnitus pitch methods made in previous studies.

	Pan et al. (2009)	Moore et al. (2010)
No. of participants	195 (128 ♂, 67 ♀)	11 (7 ♂, 4 ♀)
Type of tinnitus	No exclusions. Analyses of pitch-matching results of the tonal-type tinnitus did not reveal relationship with audiogram.	Only tonal-type.
Severity of hearing loss	No exclusions.	Generally high-frequency sloping loss with maximum loss at 8000 Hz of 75 dB HL.
Tinnitus Pitch-matching procedure	Bracketing methods used, with half octave step variations. Matching was done to the *most prominent* pitch of the tinnitus.	Loudness matches first followed by pitch-matching. Training was provided to identify octave errors.
Final pitch match	Average of three trials using the bracketing method.	Average of nine runs, tested independently by 3 experimenters. The final pitch match was chosen by asking the participant which frequency most closely matched their tinnitus.

The two studies investigated the relationship between tinnitus pitch and the audiogram.

However, only Moore et al. (2010) managed to reveal a clear relationship between the edge

frequency on the audiogram and the tinnitus pitch. The differences between the methods used

in both studies are highlighted in Table 3.2. There were similarities between Moore et al.'s

(2010) more successful method and the Tinnitus Spectrum procedure in this study. Although

Moore et al.'s (2010) method used a manual adjustment method to guide participants to

concentrate on the most prominent pitch, the participants were also asked to identify which

was the closest match out of a set of selected frequencies.

In conclusion, this pilot study was done to explore the efficiency of the Tinnitus

Spectrum method, compared to the Tinnitus Pitch-matching method in naive listeners with

normal-hearing. The Tinnitus Spectrum method is preferred to the Tinnitus Pitch-matching

method as it has been proven to have robust reliability in this pilot study. It also does not allow

premature termination of the task by ensuring all the frequencies tested are rated, and does

not assume the presence of a prominent pitch. Subsequent analyses on the Tinnitus Spectrum

will be made on the frequencies that correspond to the highest (maximum) score given by the

participants.

3.5   Statistical Analyses

This thesis focuses on comparisons between two hearing-impaired groups; one with

tinnitus and the other without tinnitus. No previous studies were reported to have investigated

cochlear function using psychophysical measurements between these two groups. Therefore, a

sample size estimate had to be based on non-tinnitus related studies to approximate the

number of participants required for each group. One such study was a psychophysical task

carried out by Kluk et al. (2006), who investigated the amount of frequency selectivity in

hearing-impaired listeners. The results of their work suggest that the changes in the

psychophysical measurements made would be small. Frequency selectivity was quantified using

Q_{10} values and the mean for one group was estimated to be around 2, with a standard deviation

of 0.75, while the estimated Q_{10} mean for the other group was 1, with a standard deviation of

0.75. The analysis produced a sample size of at least 9 in each group, with a power of 0.8 and at a significance level of 0.05 for a 2-sided analysis.

All the data collected were entered into the IBM Statistical Package for the Social Sciences (SPSS) software for analyses. Analyses were done on absolute thresholds, frequency selectivity, compression, Uncomfortable Loudness Levels and DPOAEs at all the frequencies measured. All analyses were made at 250, 500, 1000, 2000, 4000, 6000 and 8000 Hz. Arbitrary values were included in the analyses to indicate direction of extreme values. For instance, the value 100 was used to indicate absolute thresholds that were too high to be measured and values of ±100 were used to indicate the direction of off-frequency shifts that were expressed as diagonal lines in the Hearing Profiles. Arbitrary values of 200 were also used in the uncomfortable loudness level analyses to indicate the ULL thresholds may be above 110 dB SPL and above. Missing values were coded by default in SPSS. A Mann-Whitney analysis of ranks was used for conditions where extreme values had to be coded. Otherwise, the results were analysed by comparing the means in an independent t-test. A Bonferroni correction was applied to adjust the significance level ($\alpha = 0.05/n$ for n tests) where needed. For instance, where comparisons were made between 3 groups, the critical level for significance was set at $p = 0.05/ 3 = 0.0167$). Other variations of statistical tests carried out were explained in detail, in the corresponding chapters.

Chapter 4
Summary of Hearing Profiles

4.1 Hearing Profiles with similar absolute thresholds

The general aim of this thesis is to investigate if there was a difference in cochlear function between people who have tinnitus, and those without tinnitus, but with similar amounts of hearing impairment. This is an important question to answer, in order to understand the specific cochlear damages that are unique triggers of tinnitus. Basic visual comparisons, in the previous section, suggested that people with tinnitus in this study may have better frequency selectivity and compression compared to those without tinnitus. However, these observations may be influenced by different degrees of hearing loss; frequency selectivity and compression degrade with an increase in hearing loss.

Figure 4.1 compares pairs of hearing profiles with similar amounts of hearing impairment. This was done by firstly identifying hearing profiles with similar degrees of hearing loss by matching their absolute thresholds. They were then segregated into two groups; one with tinnitus and the other without tinnitus. The general impression of this simple grouping method was striking. The visual comparisons did indeed suggest a better presence of frequency selectivity and compression in the tinnitus group (left column; no tinnitus group in right column). This could be identified by the sharper IFMC shape and the steeper TMC slopes in the hearing profiles.

Tinnitus, Hearing-impaired

No Tinnitus, Hearing-impaired
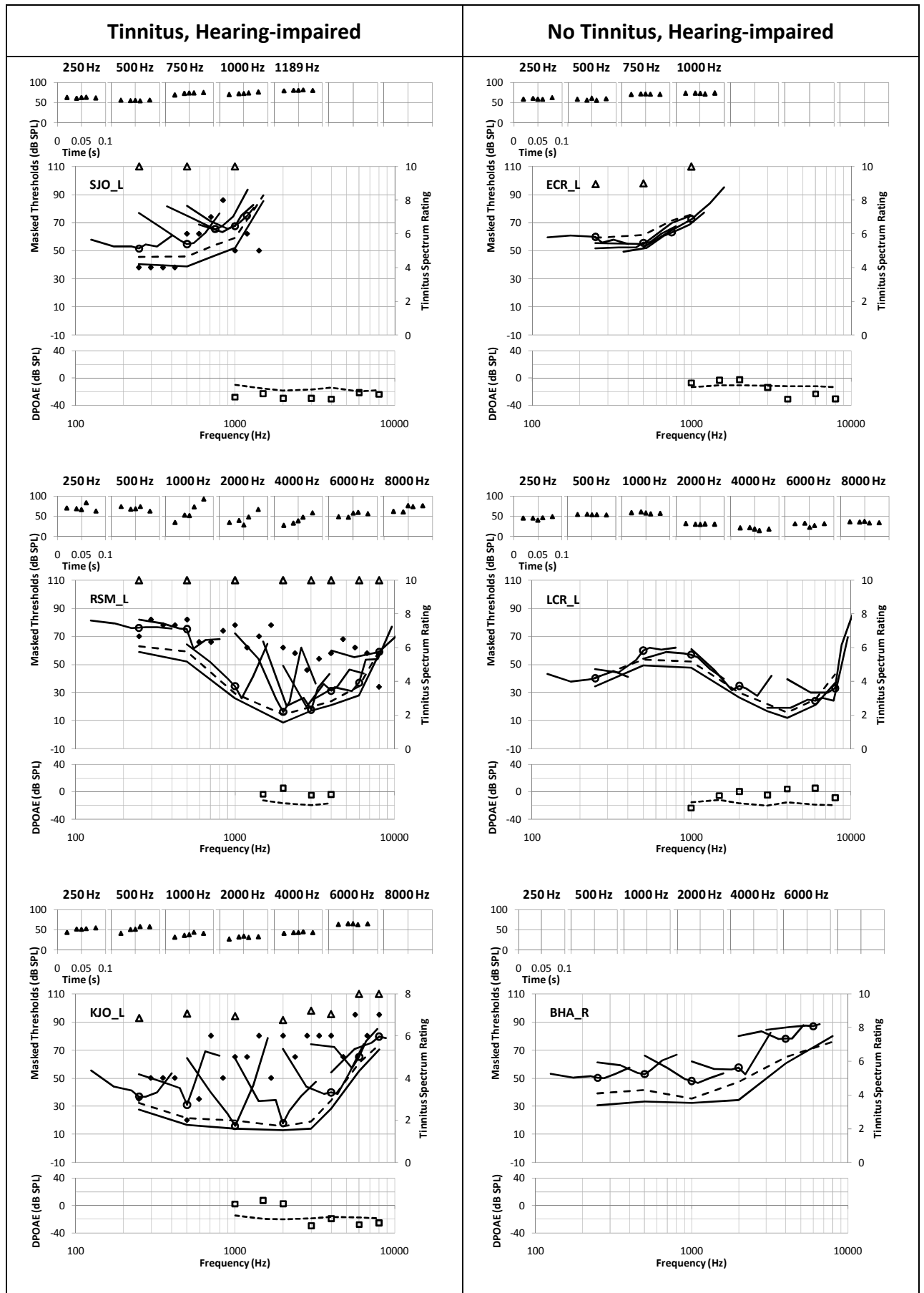
Tinnitus, Hearing-impaired
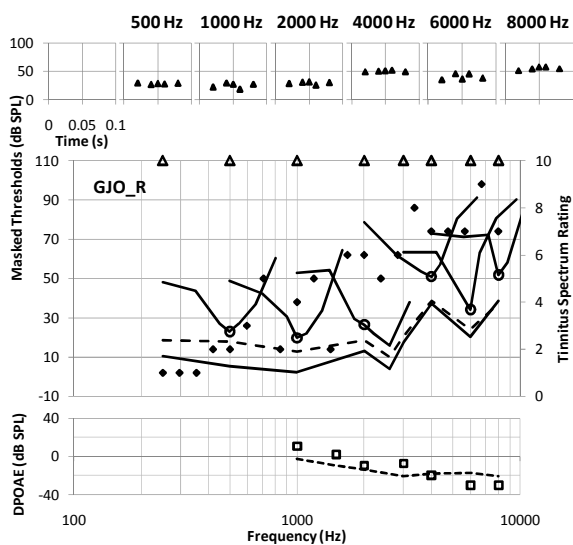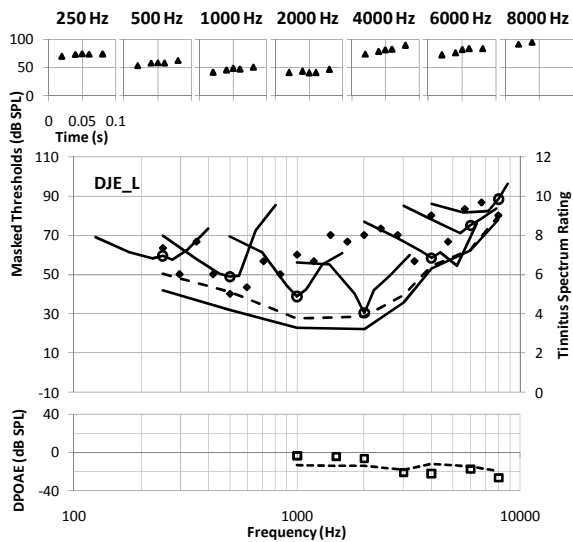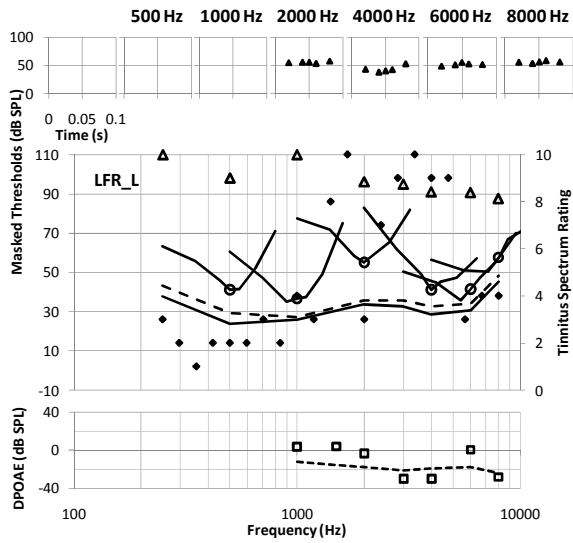
No Tinnitus, Hearing-impaired
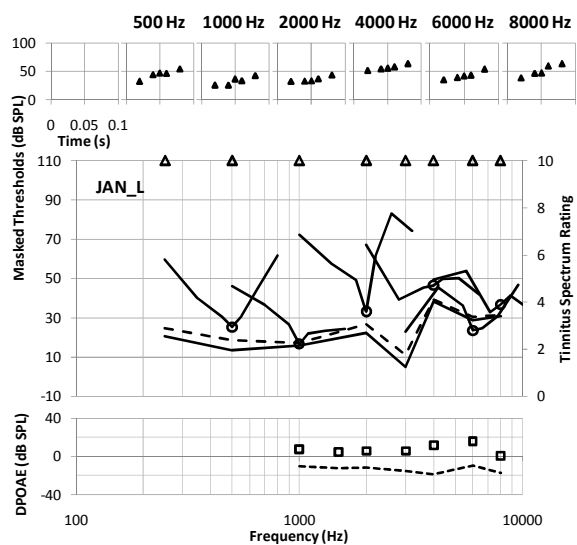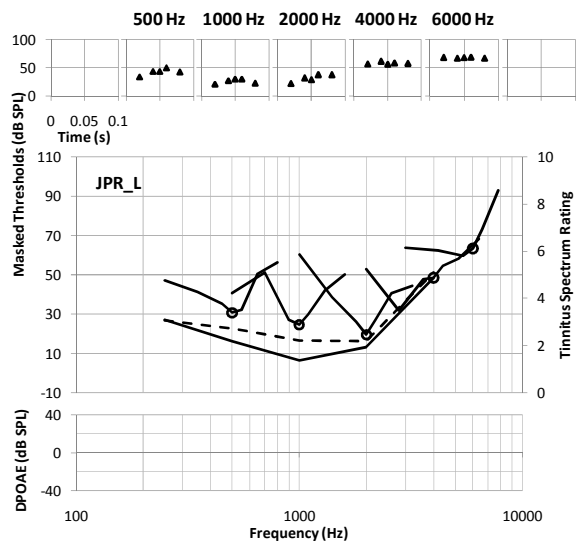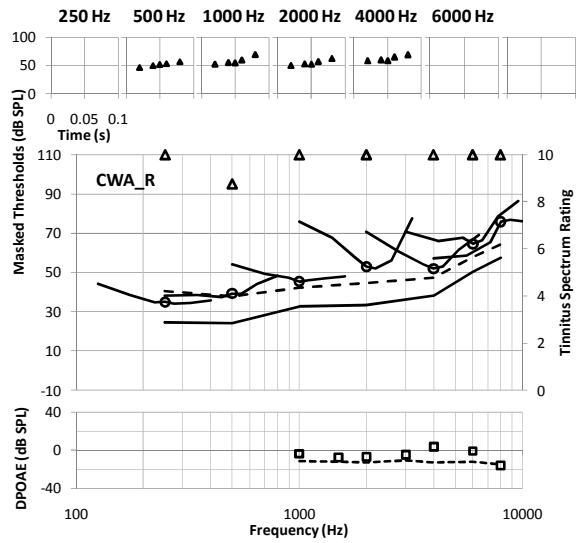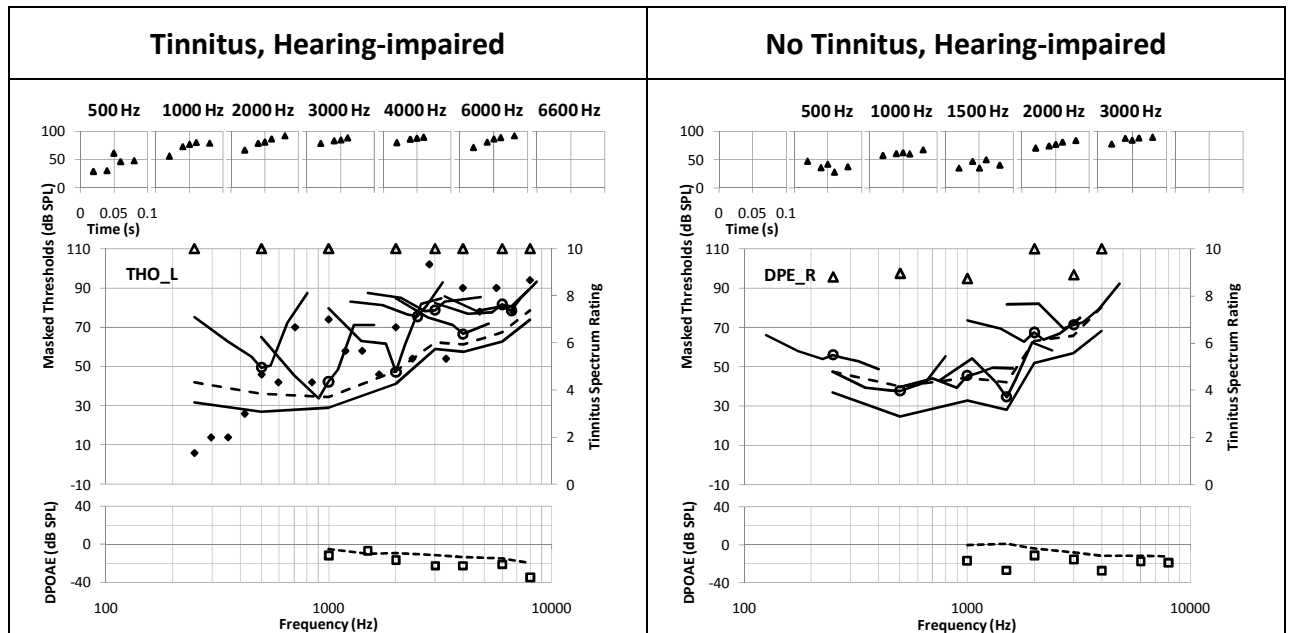
Figure 4.1: Matched pairs based on similar absolute thresholds, compared between the tinnitus group (left column) and no tinnitus group (right column). See Figure 0.1 for full description of the Hearing Profiles.

The preliminary evidence suggested distinct differences between the two hearing-impaired groups. The tinnitus group had seemingly better frequency selectivity and measures of compression compared to those without tinnitus. This is the first report that suggests the possibility of a functional outer hair cell system in people with tinnitus. Tinnitus theories are often centred on the failure of outer hair cell function as a trigger for the condition (Section 2.1.3). Subsequent chapters will make detailed comparisons between the tinnitus and no tinnitus group. The different hearing tests will be quantified and any significant differences between the two groups will be reported.

4.2   Average Hearing Profiles

The average profiles for three different groups are shown in Figure 4.2. These were obtained by averaging the psychophysical measurements across participants in a group, at different frequencies. The hearing profiles of normal-hearing individuals typically show low

absolute threshold values, sharp V-shaped IFMCs, TMCs with steep slopes and measurable

DPOAEs at most frequencies. Hearing-impaired profiles often had raised absolute thresholds at

the higher frequencies, with abnormally shaped IFMCs and shallower TMC slopes. DPOAEs in

the hearing-impaired groups were sometimes present, but in most cases, they were not

measurable.

(A) Tinnitus, hearing-impaired
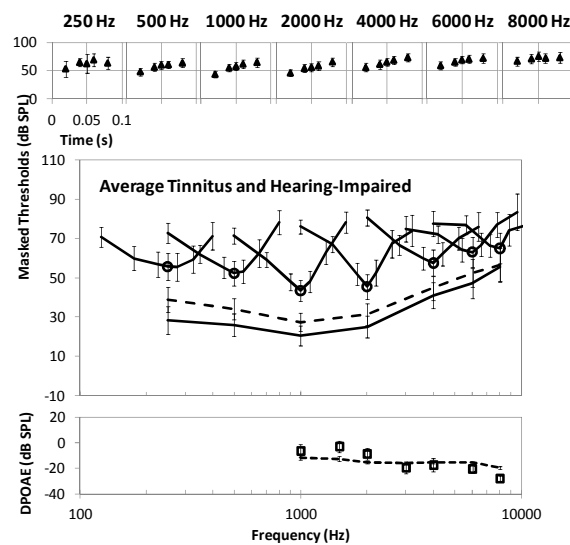
(B) No tinnitus, hearing-impaired
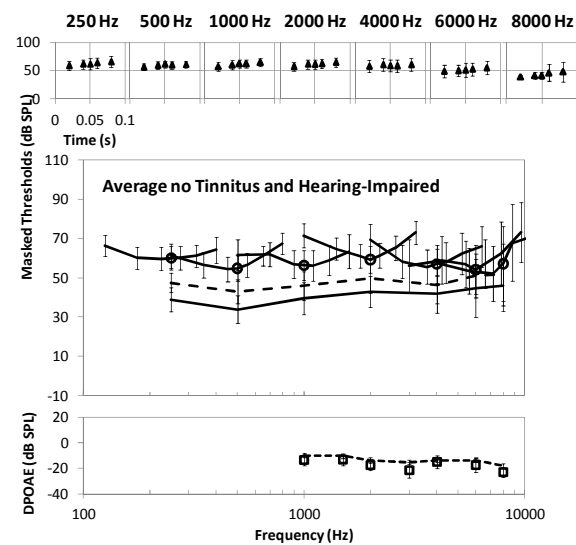
(C) Normal-hearing, no tinnitus
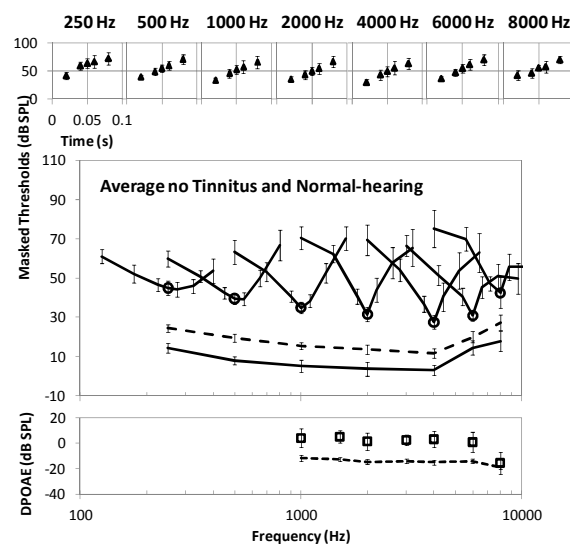
Figure 4.2: Average hearing profiles of each group (mean ± 95% C.I.). The top panel of a hearing profile represents the Temporal Masking Curve measures at various frequencies (filled triangles). The middle panel shows absolute thresholds measured using long durations (solid line, left axis) and short durations (dashed line, left axis), frequency selectivity (solid line, with probe frequency indicated by an open circle, left axis). The bottom panel shows the DPOAE responses (square) where present and the associated amount of noise (dotted line).

Chapter 5
Absolute Thresholds

Absolute thresholds are routinely measured in hearing clinics to assess the degree of hearing loss. These are made relative to average normal-hearing threshold (dB HL), and are plotted in an audiogram. Epidemiological studies often report a strong relationship between tinnitus and the presence of hearing-impairment (Davis and El Refaie, 2000), and it has been experimentally shown that they often occur together (Atherley et al., 1968; Loeb and Smith, 1967). However, the relationship between absolute thresholds (audiograms) and tinnitus is not straightforward. Firstly, although tinnitus sufferers often have impaired hearing, there are variations on the types of hearing loss present (Meikle, 1995). Secondly, not everyone with hearing loss has tinnitus (König et al., 2006) and thirdly, some people with clinically normal-hearing also have tinnitus (Kehrle et al., 2008; Shiomi et al., 1997). However, studies have reported the presence of previously undetected hearing losses in people with seemingly normal-hearing (Mitchell and Creedon, 1995; Shiomi et al., 1997; Weisz et al., 2006). This further strengthens the relationship between hearing loss and tinnitus, but it does not identify what type of impairment is unique to people with tinnitus.

The total amount of hearing loss has been proposed to reflect a combination of outer and inner hair cell defects (Moore and Glasberg, 2004; Moore et al., 2000). Studies by Hawkins and colleagues (Hawkins et al., 1976; Stebbins et al., 1979) investigated variations of outer and inner hair cell damage on hearing thresholds in animals that were acoustically traumatised (120 dB SPL noise). They observed that outer hair cell loss correlated with absolute threshold shifts of 50 dB SPL or less. Inner hair cell loss, on the other hand, was thought to be associated with

losses greater than 50 dB SPL. Although the delineation between the two hair cell systems was proposed, the authors admitted that the concept was oversimplified because combinations of damage are also possible.

König et al.'s (2006) study is the only known study, to date, to have exclusively compared absolute threshold measurements between hearing-impaired groups (one with tinnitus, the other without tinnitus). Previous studies were interested in the core differences between tinnitus and no tinnitus group, regardless of the amount of hearing loss present. König et al. (2006) analysed the area under the audiogram to estimate the amount of hearing loss present. This differed from the normal way to describe the amount of hearing loss on an audiogram, which is based on the average thresholds at 250, 500, 1000, 2000 and 4000 Hz (Audiology, 2004). The authors reported that both hearing-impaired groups had high-frequency hearing loss. The differences at the highest and lowest frequencies measured were not significant. However, the amount of hearing loss was greater in the group without tinnitus, as identified by the methods used in König et al.'s (2006) study. This chapter quantifies hearing impairment with König et al.'s (2006) method (area under audiogram) and by averaging across frequencies.

A number of analyses were carried out in this section. Firstly, the absolute thresholds of the normal-hearing group were compared against the international standards to check that no systemic errors in the measurements were present. Next, the average absolute thresholds of the tinnitus group were compared against the average Tinnitus Spectrum to highlight the relationship between tinnitus and hearing loss. The absolute threshold measurements were then quantified to determine the amount of hearing loss, and comparisons between the two hearing-impaired groups were made. Procedures to carry out absolute threshold measurements were detailed in Section 3.4.1.

5.1 Normal-hearing

This section compares the absolute thresholds of the normal-hearing group against the international standard to check that no systemic errors were present in the measurements made. The absolute thresholds of the normal-hearing group were plotted across the frequencies measured (Figure 5.1). The results were compared against the international Reference Equivalent Threshold Sound Pressure Level (RETSPL) standards, which were measured with circumaural headphones (BSI, 2004).
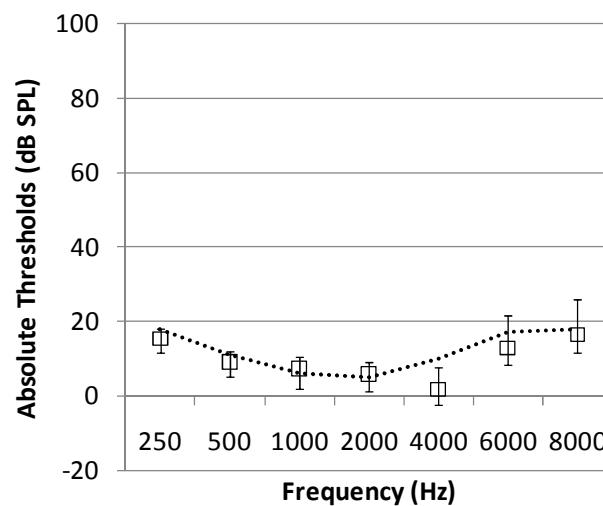
Figure 5.1: Absolute thresholds (median ± inter quartile range) of the normal-hearing group shown by the open squares. The dotted line represents the RETSPL for circumaural headphones.

This comparison helped establish the boundary for 'normal-hearing'. Hearing-impairment in this study is defined as deviations that are more than +20 dB SPL worse than the average normal-hearing measured in this study. The absolute threshold values in the normal-hearing group has a 'bowled-shaped' function, which means that the thresholds in the mid-frequencies are much lower than the lowest and highest frequencies measured. This pattern is

typical of normal-hearing because the outer/ middle ear is more efficient at transmitting

sounds in the mid-frequency regions (500 to 4000 Hz) (Pickles, 2008).

5.2   Tinnitus Spectrum and Absolute Thresholds

In this section, the relationship between absolute thresholds in hearing-impaired

tinnitus sufferers and their Tinnitus Spectrum were investigated. The ratings on the Tinnitus

Spectrum indicate how different pure tones at various frequencies contribute to the percept of

tinnitus. High ratings on the Tinnitus Spectrum suggest that the frequency of the pure tone at is

perceived to be very similar to the tinnitus heard, while low rating suggest the opposite.
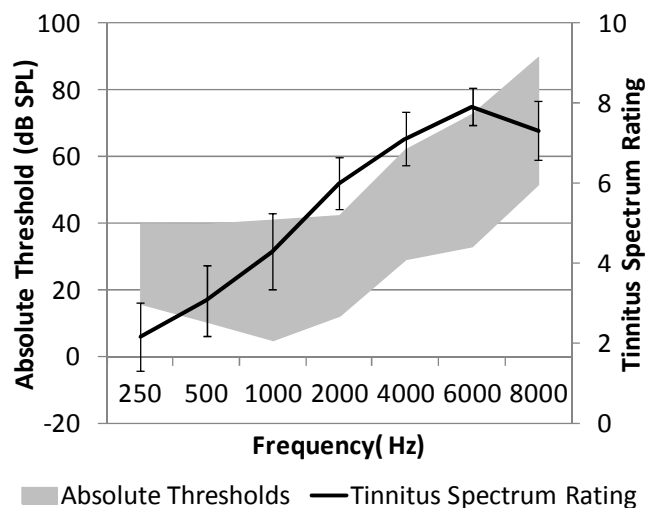
Figure 5.2: Average absolute thresholds (grey area indicating inter-quartile range, left axis) for hearing-impaired listeners with tinnitus, measured at different frequencies. The average maximum ratings on the Tinnitus Spectrum task for the tinnitus group (mean ± 95% C.I., right axis) is shown as a solid line.

The results showed that the average maximum ratings of the Tinnitus Spectrum, across

all listeners in the tinnitus group, reached a plateau between 4000 Hz to 8000 Hz. This

coincided with regions that had raised absolute thresholds (Figure 5.2). The results offer

support for a relationship between the presence of tinnitus, as assessed by the Tinnitus

Spectrum method, and damage to the hearing pathway (Noreña et al., 2002).

Hearing loss was quantified in three ways; (1) calculation of the average hearing loss

across frequency, (2) investigation of the trend of hearing loss across frequency and (3)

calculation of the area under the absolute thresholds. It was not possible to measure absolute

thresholds in some hearing-impaired people because the levels exceeded the maximum limit

set by the computer program. In such instances, the missing values were coded as '100', as an

indication that the threshold may be 100 dB SPL or higher. Absolute threshold measurements

were analysed at clinically tested frequencies of 250, 500, 1000, 2000, 4000 and 8000 Hz. Non

parametric analyses were carried out using the Mann-Whitney test between the two hearing-

impaired groups.

5.3 Average absolute thresholds between groups

Quantification of hearing loss is carried out in this section by calculating the average

absolute threshold across clinically tested frequencies of 250, 500, 1000, 2000, 4000 and 8000

Hz (Figure 5.3). A two-tailed analysis was used to test if the differences between the two

hearing-impaired groups were significant. The difference between the median threshold of the

no tinnitus and tinnitus group was only 4.6 dB SPL. This difference was not found to be

significantly different between the two hearing-impaired groups (z = -1.67, p = 0.10, two-tailed).

Two outliers were present in the tinnitus group (PTO_R and SJO_L) because their average
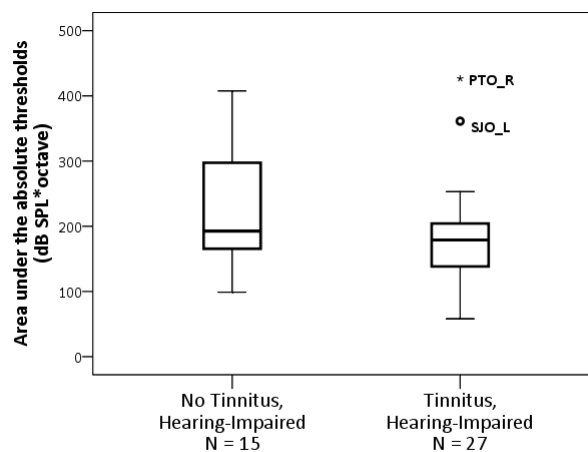
absolute thresholds were much higher than the group average.
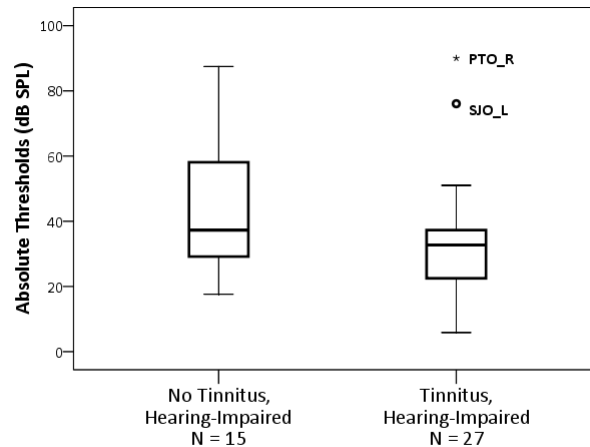
Figure 5.3: Average absolute thresholds (median ± inter quartile range) between hearing-impaired listeners without tinnitus and hearing-impaired listeners with tinnitus.

5.4   Average absolute thresholds at different frequencies

This section investigates the trend of absolute threshold values across different probe frequencies, between the two hearing-impaired groups. The tinnitus and no tinnitus group both had typical high-frequency loss. A linear regression lines were plotted across frequency for each group. The tinnitus group was found to have a steeper high-frequency loss (b = 0.007) compared to the no tinnitus group (b = 0.005). This observation was consistent with König et al.'s (2006) findings who also reported that the no tinnitus group in their study, had a more gradual sloping function compared to their tinnitus group. However, in this study, the difference between these two trends were not found to be significant (t(5) = -0.013, p > 0.05, two-tailed). More in-depth investigation into the slopes of the absolute thresholds across octave frequencies will be carried out in Chapter 6.
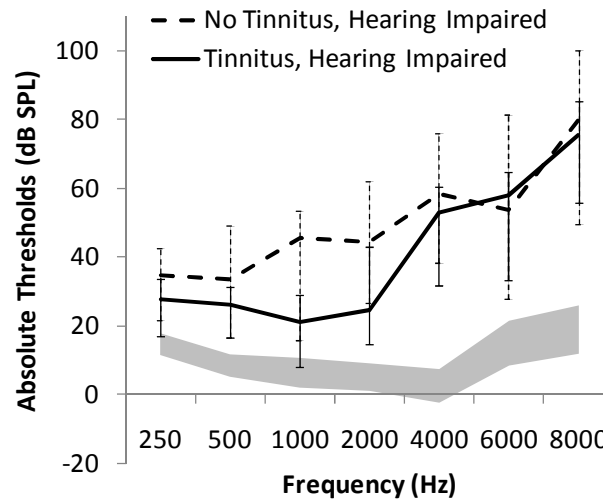
Figure 5.4: Average absolute threshold (median ± inter quartile range) at different frequencies for hearing-impaired listeners with tinnitus (solid line) and hearing-impaired listeners without tinnitus (dashed line). The grey area represents the average absolute thresholds (median ± inter quartile range) for the normal-hearing group.

Table 5.1: Statistical p values of group differences for average absolute threshold measurements at each frequency bin. Criteria for significance is at p = 0.05/7 = 0.0071.

Group differences	250	500	1000	2000	4000	6000	8000
p-value (2-tailed)	0.0855	0.1682	0.0152	0.0261	0.4327	0.9626	0.6093

The median absolute thresholds for both the tinnitus and no tinnitus group were below 50 dB SPL between 250 Hz and 2000 Hz, and above 50 dB SPL between 4000 Hz and 8000 Hz. According to Hawkins and colleagues' interpretation(Hawkins et al., 1976; Stebbins et al., 1979), absolute threshold loss of up to 50 dB SPL are proposed to be associated with outer hair cell defects, while losses that are more than 50 dB SPL are proposed to be due to inner hair cell defects. However, various combinations of defects could exist and it is not possible to identify the contribution from each individual hair cell system from absolute threshold measurements alone (Moore and Glasberg, 2004; Moore et al., 2000). Table 5.1 describes exploratory analyses to investigate group differences at each frequency bin. Readjustments for multiple comparisons

were carried out using Bonferroni correction, with the new criteria for significance at $p = 0.0071$.

5.5   Area under absolute thresholds

König et al. (2006) quantified the degree of hearing loss present by estimating the area under the audiogram. The measurements were quantified as overall hearing loss, and measured in dB*octaves. The authors reported that the no tinnitus group in their study had a significantly greater amount of hearing loss compared to the tinnitus group. The difference between the groups, in their study, was estimated to be 42 dB*octave ($p = 0.0006$). Sereda et al. (2011) also used similar methods to quantify the amount of hearing loss present but did not make any comparison between hearing-impaired listeners with tinnitus and hearing-impaired listeners without tinnitus.

Figure 5.5: Average area under the absolute thresholds (median ± inter quartile range) for hearing-impaired listeners without tinnitus and hearing-impaired listeners with tinnitus.

König et al. (2006)'s method is adopted in this section as an alternative measure of the amount of hearing impairment present. The area under the absolute thresholds was calculated

in octave steps, starting from 250 Hz. A larger area (higher number) suggests a greater amount of hearing loss while a smaller area suggests a less severe amount of hearing loss. Unlike the results reported by König et al. (2006), the median area difference between the two groups, was found to be much smaller, at 26 dB SPL*octave. This was found to be significantly different between the two groups (z = -1.82, p = 0.036, one-tailed). The same two outliers (PTO_R and SJO_L) in Section 5.3 were present in this analysis, because they both had significant amounts of hearing loss compared to the group average. In summary, only one out of the three methods used to estimate the extent of hearing impairment present in the two hearing-impaired groups were successful at uncovering significant differences between the two hearing-impaired groups.

5.6 Discussion

The aim of this section was to investigate the differences in the amount of hearing loss present in the tinnitus and no tinnitus group. This was done by (1) calculation of the average hearing loss across frequency, (2) investigation of the trend of hearing loss across frequency and (3) calculation of the area under the absolute thresholds. Previous reports by König et al. (2006) suggested a greater amount of hearing loss in people without tinnitus, despite having similar amounts of losses at the highest and lowest frequencies measured. Their analyses involved calculation of the area under the absolute thresholds and were conducted with a greater number of measurement points (10 frequencies between 125 Hz and 8000 Hz). The replication of their work in this study with the same number of measurement points conducted in clinics (7 frequencies between 250 Hz and 8000 Hz, at 7 frequencies), uncovered significant differences between the two groups.

Comparisons made between absolute threshold and the Tinnitus Spectrum method in the tinnitus group replicated the results of studies that also observed that the high ratings on the Tinnitus Spectrum were located in regions with raised thresholds (Noreña et al., 2002; Sereda et al., 2011). The results in this chapter highlights the already established belief that tinnitus is strongly linked to the presence of hearing impairment.

5.7   Conclusions

1.   The absolute threshold measurements in the normal-hearing group were comparable with international standard. The presence of hearing-impairment is defined to be +20 dB SPL worse than the average normal-hearing thresholds.

2.   The perception of tinnitus coincided with regions with raised thresholds, confirming that this form of *'cochlear tinnitus'* occurs with the existence of damage that may happen in the inner ear.

3.   The analyses performed between the two hearing-impaired groups included (1) average group comparison, (2) trend comparison across individual frequencies and (3) area under the absolute thresholds. Only the analyses that calculated area under the absolute thresholds suggested that hearing-impaired listeners without tinnitus had a greater amount of hearing loss compared to hearing-impaired listeners who had tinnitus.

Chapter 6
Threshold slopes

Tinnitus is thought to be related to the disparity between normal and abnormal regions in the cochlea (Kiang et al., 1970). The contrast between normal and impaired function of regions in the cochlea are hypothesised to disrupt the pattern of spontaneous activity in the area, leading to abnormal neural patterns that the brain interprets as tinnitus. This is often illustrated in an audiogram as an 'edge' where normal thresholds start to deteriorate. The 'Edge Effect' theory has been investigated in terms of *threshold slopes* ('slope of the audiogram'). The theory predicts that people with tinnitus will have steeper sloping audiograms. The 'Edge Effect' theory is supported by observations of plasticity in the cortical areas of acoustically traumatised animals (Eggermont and Roberts, 2004). Eggermont and Roberts (2004) proposed that the over-representation of the tonotopic map, close to the 'edge' of hearing will give rise to tinnitus.

However, the relationship between the slope of the audiogram and the presence of tinnitus has not always been straightforward. Firstly, only *some* tinnitus sufferers have steeply-sloping audiograms (Pan et al., 2009). Secondly, the pitch of tinnitus is not always perceived at the 'edge' of hearing loss (Penner, 1983; Tyler and Conrad-Armes, 1983a). The reasons for this latter observation may be related to the assumptions made about tinnitus pitch and difficulties faced when making pitch measurements, which were discussed in Sections 2.5, 3.4.5 and 3.4.6. These two issues, relating threshold slopes and tinnitus, will be addressed in this chapter and the results compared with other studies.

König et al. (2006) investigated the presence of threshold slopes in hearing-impaired groups; one with tinnitus, and the other without tinnitus. The no tinnitus group was reported to

have greater hearing loss (also see Chapter 5), but shallower *maximum* threshold slopes than those with tinnitus. These *maximum* threshold slopes were obtained by finding the *maximum* difference in absolute threshold measurements that were an octave apart on the audiogram. König et al.'s (2006) method is implemented in this chapter to check if the same observations were reproducible. This method is preferred over other methods of estimating threshold slopes (Pan et al., 2009; Sereda et al., 2011) because (1) it does not assume that the steepest slope should always occur adjacent to the 'edge' of hearing loss; rather, it searches for the maximum amount of disparity between adjacent regions. (2) 'Steepness' is defined relative to variations in the individuals' audiograms, and not to a specified numerical value.

This chapter also investigates the relationship between the Tinnitus Spectrum and the 'edge' of hearing loss. Noreña et al. (2002) was the only study that reported robust relationship between the Tinnitus Spectrum and hearing impairment. However, Sereda et al. (2011) has since made similar investigations. Sereda et al. (2011) failed to find a strong relationship between the 'edge' of hearing loss and the percept of tinnitus. Rather, they observed that tinnitus was mostly perceived in regions with impaired hearing. The results presented in this chapter will be compared to those obtained by Sereda et al. (2011). Absolute thresholds were analysed in octave steps of 250, 500, 1000, 2000, 4000 and 8000 Hz. The means between groups were compared with an independent t-test.

6.1   Average Maximum Threshold Slopes between groups

The 'Edge Effect' theory predicts that tinnitus sufferers will have steeper threshold slopes compared to those without tinnitus. This section investigates this hypothesis in hearing-impaired individuals, with or without tinnitus. Maximum threshold slopes were calculated by finding the *maximum* difference in absolute threshold measurements that are an octave apart,

across frequencies of 250, 500, 1000, 2000, 4000 and 8000 Hz. These were a smaller set of values used compared to König et al.'s (2006) study who made measurements across smaller frequency intervals (10 frequencies between 125 Hz and 8000 Hz). In their study, they reported the presence of steeper slopes in their tinnitus group (52.9 dB/ octave), compared to their no tinnitus group (43.1 dB/ octave) (see Figure 6.1). The difference between their two groups (9.8 dB/ octave) was significant (p = 0.002).

The analyses in this section (Figure 6.1) also showed that the tinnitus group had steeper slopes (33.4 dB SPL/ octave) compared to the no tinnitus group (24.9 dB SPL/ octave). The difference between the two groups (6.1 dB SPL/ octave) was significant (t(40) = -1.73, p = 0.046, one-tailed).
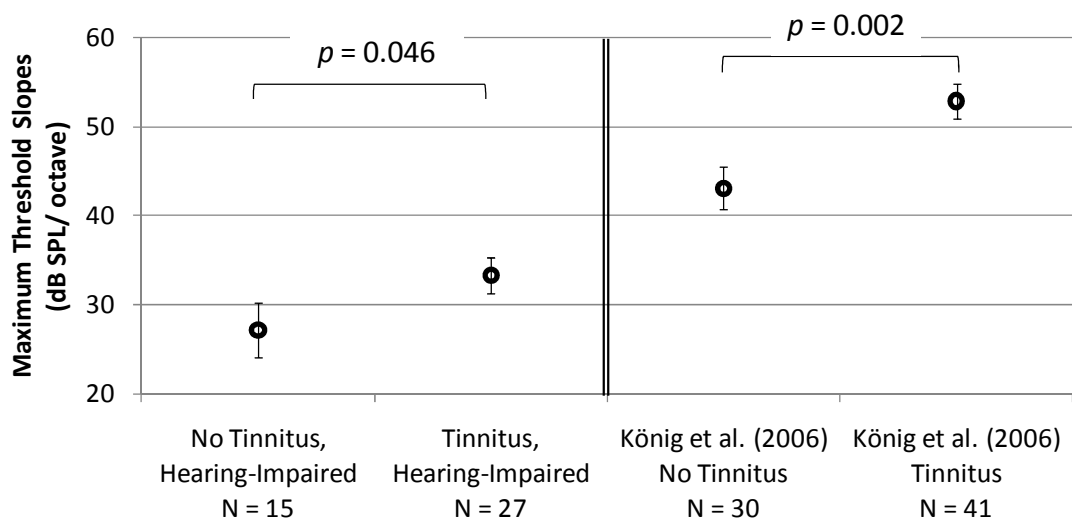
Figure 6.1: The left panel represents maximum threshold slopes (mean ± 1 s.e.m) for hearing-impaired listeners without tinnitus and hearing-impaired listeners with tinnitus that were measured in this study. The right panel represents the results presented in König et al.'s (2006) study.

6.2   'Edge' of hearing loss and Tinnitus Spectrum

The 'Edge Effect' theory also predicts that the pitch of the tinnitus should occur at the point at which a disparity between 'normal' and 'impaired' is present. In most individuals with a high-frequency hearing loss, this 'edge' is defined as the point at which absolute thresholds start deteriorating into the 'impaired' region (Sereda et al., 2011). Studies that investigated the relationship between this 'edge' and the presence of tinnitus pitch reported inconsistencies and large variability in obtaining repeatable pitch measurements. The main reason for this involves the difficulties to obtain repeatable measures of pitch, which were discussed in Section 2.5. Preferences for the Tinnitus Spectrum method were highlighted in Sections 3.4.5 and 3.4.6.

In Sereda et al.'s study, (2011), they quantified absolute thresholds using a broken stick function to identify the (1) 'edge', (2) slope and (3) degree of hearing loss. The authors used the Tinnitus Spectrum method to quantify the tinnitus heard. They failed to find a robust relationship between the 'edge' and the presence of tinnitus. However, they reported a consistent relationship between the tinnitus heard and the region where hearing loss was present. Their findings supported similar observations reported by Roberts et al. (2006; 2008), and first reported by Noreña et al. (2002). Sereda et al. (2011) quantified the Tinnitus Spectrum in two ways. In the first method, the frequency with the highest rating on the Tinnitus Spectrum that was also closest to the 'edge' of hearing represented the tinnitus percept. The second method implemented a weighting system based on the Borg scale (Borg and Borg, 2001), to investigate the effect of bandwidth.

The analyses conducted in this section differed from previous studies in a number of ways. Firstly, this study assumes that cochlear defects are the main trigger of tinnitus. All other forms of non-auditory triggers are excluded in the analyses. Secondly, the frequencies measured for this analysis are the same as those typically obtained in hearing clinics (250, 500,

1000, 2000, 4000 and 8000 Hz). This was a much smaller frequency set compared to Sereda et al.'s (2011) study who made measurements between 500 Hz to 12000 Hz (11 frequencies). Thirdly, the tinnitus percept was quantified in this study by identifying the frequency with the maximum rating on the Tinnitus Spectrum. The average frequency is calculated if more than one frequency has a maximum rating. This is a novel method of using the Tinnitus Spectrum to quantify the percept of tinnitus.
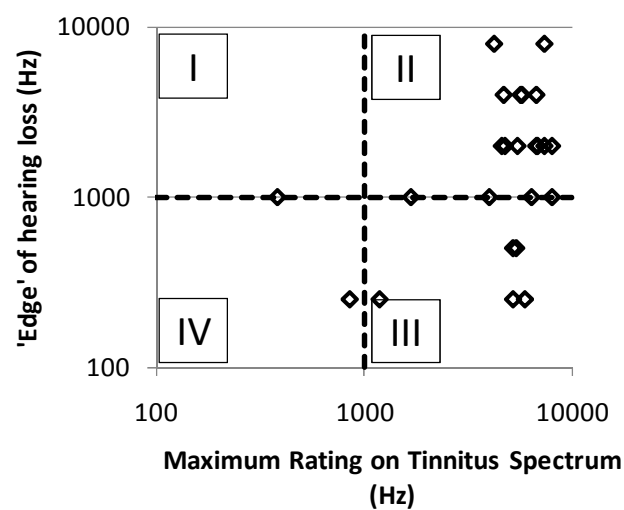
Figure 6.2: The average maximum rating on the Tinnitus Spectrum task plotted against the 'edge' of hearing loss for hearing-impaired listeners with tinnitus. Each point represents individual results.

Figure 6.2 describes the relationship between the percept of tinnitus and the 'edge' of hearing loss. The graph is arbitrarily divided into four quadrants, with frequencies below 1000 Hz classified as 'low frequencies' and those above 1000 Hz, as 'high frequencies'. The 'Edge Effect' hypothesis would predict that tinnitus sufferers perceive their tinnitus close to the 'edge' of hearing loss (Quadrants II and IV). Any presence of data points in Quadrants I and III contradicts the theory. The results showed that the majority of tinnitus sufferers who have high-frequency hearing loss also perceive high-pitched tinnitus (Quadrant II). Some participants

with low frequency 'edge' also perceive low-pitched tinnitus (Quadrant IV). However, some perceived their tinnitus at a higher pitch than their 'edge' of hearing loss (Quadrant III). This corresponds with regions where they have hearing loss instead, and contradicts the assumptions made by the 'Edge Effect' theory. Quadrant I was empty, suggesting that the chances of perceiving low-pitch tinnitus in the presence of high-frequency hearing loss are minimal. The results suggest some support for the 'Edge Effect' theory. However, the results also support previous observations that suggest a stronger relationship between tinnitus and regions of impaired hearing (Noreña et al., 2002; Roberts et al., 2006; Roberts et al., 2008; Sereda et al., 2011).

6.3   Discussion

The aim of this chapter was to test the validity of the 'Edge Effect' theory detailed in Section 2.2. Whereas the previous chapter investigated the relationship between the degree of hearing loss and tinnitus, this chapter addresses specific hypotheses presented by the 'Edge Effect' theory. The first prediction made by the 'Edge Effect' theory, is that tinnitus sufferers will have steeper slopes in their absolute threshold function. This is because the 'Edge Effect' theory predicts the presence of tinnitus in regions with a sudden transition between 'normal' and 'impaired'. The analyses performed in this chapter supported this suggestion; *steeper* absolute threshold slopes were found in people with tinnitus. These slopes, however, were found to be overall shallower in this study compared to the steeper slopes reported in König et al.'s (2006) study. One explanation for this is the different participant population used. All of the participants in König et al.'s (2006) study reported a history of work-related noise-induced trauma, whereas only some of the hearing-impaired population studied in this thesis reported a history of noise damage. It is possible that very steep slopes are a characteristic feature of

noise-induced trauma, but very steep slopes may not necessarily always manifest itself in the audiograms of people with tinnitus. The observation that hearing-impaired listeners with tinnitus have *steeper* slopes than those who are only hearing-impaired supports the 'Edge Effect' theory of regions with sudden transitions between 'normal' and 'impaired'. The exact type of cochlear damage that creates this typical pattern, however, is still unknown.

The second prediction made by the 'Edge Effect' theory proposes that tinnitus is heard at the 'edge' of hearing loss (Kiang et al., 1970). This has been supported by physiological studies that propose plastic readjustments in central regions that result in an over-representation of the 'edge' frequency in the tonotopic map (Eggermont and Roberts, 2004). There was some support for the predictions of the 'Edge Effect' theory. However, some individuals also perceived their tinnitus at frequency regions where hearing loss was present, instead of at the transition from normal to impaired regions (Noreña et al., 2002; Roberts et al., 2006; Roberts et al., 2008; Sereda et al., 2011). The effect of the 'bandwidth' of tinnitus, may account for some of the variation away from the 'edge' of hearing loss (Sereda et al., 2011). However, the presence of different 'bandwidths' of tinnitus itself, suggest that the 'Edge Effect' may not be the only explanation for tinnitus. An added complication in the attempt to find a straightforward relationship between the 'pitch' of tinnitus and the 'edge' frequency using the Tinnitus Spectrum method arises when multiple peaks are present in the Tinnitus Spectrum. The presence of multiple peaks were seen in some participants and were analysed by calculating the average of the peaks obtained, which could account for some of the errors present.

Although the presence of tinnitus has shown to be strongly related to hearing loss, it is still unclear what mechanisms are responsible for triggering the condition. This is because hearing impairment can be accounted for by different types of damage in the cochlea (Section

2.1.2). Moore et al (2004a), for instance, proposed that the total amount of hearing impairment can consist of damage to both outer and inner hair cell systems. Damage to inner hair cells has been shown to reduce the total amount of spontaneous activity in the auditory nerve, which is mediated by the loss of nerve fibres (Kujawa and Liberman, 2009). The loss of outer hair cells, however, has little or no impact on the amount of spontaneous activity present in the auditory nerve (Dallos and Harris, 1978), although it affects the acoustically driven activity in the auditory nerve. Absolute thresholds reflect the summation of activity along the auditory pathway. It is thus not possible to decipher what type of cochlear damage causes the disparity between normal and abnormal regions in the cochlea from absolute threshold measurements alone.

6.4   Conclusions

1. The analyses of the threshold slopes in this section showed that people with tinnitus have, on average, steeper sections on their audiograms compared to those without tinnitus.

2. In most cases, the perception of tinnitus was related to the region where hearing loss is present, and not to the 'edge' of hearing loss.

3. It is not possible to speculate which structures in the cochlea may contribute to the perception of tinnitus from absolute threshold measurements alone without further investigation

Chapter 7
Threshold Duration Difference

Threshold duration differences relate to the difference of thresholds of long and short duration tones. Long duration tones are detected at lower intensities (lower absolute thresholds) while short duration tones are detected at higher intensities. This relationship is true for tones with durations of up to 200 msec. Garner et al. (1947) explains this phenomenon by suggesting that the ear integrates the amount of energy over the duration of the detection ('temporal integration'). An alternative suggestion is that the longer stimulus duration provides more detection opportunities ('multiple looks') (Viemeister and Wakefield, 1991; Viemeister et al., 1992). This threshold duration difference is reportedly reduced in most, but not all cases of hearing impairment (Meddis and Lecluyse, 2011).

Sanders et al. (1971) proposed the use of threshold duration differences as a diagnostic method to differentiate between cochlear and retrocochlear pathologies. They observed that the group with retrocochlear disorders (eight nerve lesions) had threshold duration differences that were comparable to those with normal-hearing. The group with suspected cochlear disorders (mostly Ménière's Disease), however, had smaller threshold duration differences. Unfortunately, subsequent studies were unable to reliably replicate the observations, and the use of threshold duration differences as a diagnostic tool was no longer pursued (Olsen, 1987).

The failure to find consistent differences between cochlear and retrocochlear pathologies could be due to the way the different pathologies were grouped. In previous studies, Ménière's Disease was often considered a cochlear pathology and eight nerve lesions were allocated to the retrocochlear group. However, dysfunction of the spiral ganglion cells has

recently been implicated in Ménière's Disease (Lefebvre et al., 1990; Nadol et al., 1995). This would suggest that Ménière's Disease have both cochlear and retrocochlear defects, and could explain the large amount of overlap found between the two groups in early threshold duration difference studies (Olsen et al., 1974).

The use of threshold duration differences as a predictor for different cochlear pathologies has been revived by more recent studies (Heinz and Young, 2004; Heinz et al., 2005; Meddis and Lecluyse, 2011). Reduction of threshold duration differences has been suggested to be a response of the loss of cochlear nonlinearity (Moore, 2007; Ruggero et al., 1997). Threshold detection is assumed a response to a fixed number of synchronous spikes in the auditory nerve. The loss of cochlear nonlinearity has been suggested to result in a steeper rate-level function in the auditory nerve. This is illustrated in Figure 7.1. In this schematic, short duration tones require a higher intensity to be heard, while longer duration tones require a lower number of spikes. These will result in *large* threshold duration differences on a *shallower* rate-level function but smaller threshold duration differences on steeper rate-level functions.

Heinz and Young (2004; 2005), however, suggested an alternative explanation for steep rate-level functions. They hypothesised that inner hair cell damage may also affect the rate-level function. In their study, neural tuning curves and rate-versus-level function of the auditory nerve were recorded in acoustically traumatised cats. The authors observed that auditory nerve responses with sharp tuning (impaired inner hair cell function) had shallower rate-level functions (which would predict *larger* threshold duration differences). On the other hand, the presence of broad tuning (impaired outer hair cell function) corresponded to steeper rate-level functions (*smaller* threshold duration differences).
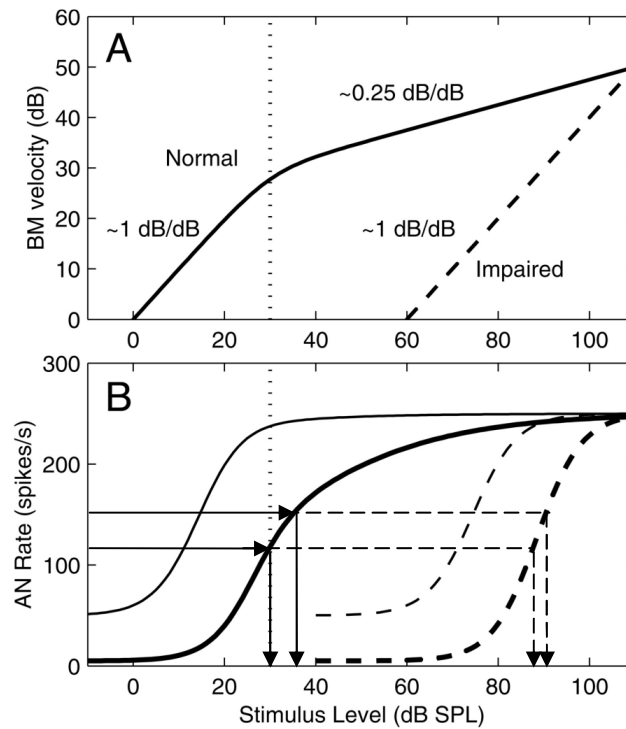
Figure 7.1: Schematic of response growth with sound level, adapted from Heinz et al. (2004). Horizontal arrows indicate the amount of (A) basilar membrane vibration and (B) rate of auditory nerve spikes required to detect long and short tones. Solid lines represent normal-hearing, while dashed lines represent impairment. Distance between vertical arrows estimate the threshold duration difference in a shallow rate-level function (solid vertical arrowed line) and a steep rate-level function (dashed vertical arrowed line).

Meddis and Lecluyse (2011) recently proposed the use of threshold duration functions to discriminate between different types of hearing loss. They measured threshold duration differences and psychometric functions in normal and hearing-impaired groups. The authors were able to use a probabilistic model to demonstrate a link between the two functions; *steeper* psychometric functions were associated with *smaller* threshold duration differences, while shallower psychometric function demonstrated larger threshold duration differences. Meddis and Lecluyse (2011) observed that only *some* of their hearing-impaired participants had steep psychometric functions. This contradicts the hypothesis that hearing-impairment is *always* associated with steep psychometric functions and smaller threshold duration differences.

Threshold duration differences comparisons between hearing-impaired groups, with or without tinnitus, have never been previously reported in the literature. In this thesis, it is proposed that tinnitus and no tinnitus group may have different inner ear pathologies. Kiang at al. (1970) has suggested that the disruption of normal spontaneous activity acts as a trigger for tinnitus (Section 2.2). If so, this disruption may be mostly triggered by inner hair cell dysfunction, rather than impairment to the outer hair cells (Dallos and Harris, 1978; Wang et al., 1997). However, other tinnitus theories (Section 2.1.3) implicate damaged outer hair cell as a trigger of tinnitus (Jastreboff, 1990). It is unclear what forms of cochlear pathologies are uniquely linked with tinnitus, and it is the aim of this thesis to investigate possible differences between the two hearing-impaired groups. Inner hair cell damage is classified as a 'retrocochlear' disorder in this chapter because this defect has been shown to cause subsequent neural degeneration in animals (Kujawa and Liberman, 2009). Outer hair cell dysfunction, on the other hand, will be classified as 'cochlear' disorder.

Threshold duration differences were calculated by finding the difference between the absolute thresholds of the 250 msec and 16 msec tones measured in this study. These were analysed and compared between the two hearing-impaired groups. Analysis was performed at 250, 500, 1000, 2000, 4000, 6000 and 8000 Hz. The differences between the two groups were assessed statistically using an independent t-test.

7.1   Average threshold duration difference between groups

In this section, the threshold duration differences were averaged over 250, 500, 1000, 2000, 4000, 6000 and 8000 Hz (Figure 7.2). The tinnitus group was found to have larger threshold duration differences (5 dB) compared to the no tinnitus group (3.66 dB SPL). The mean values between the two groups were found to be significantly different ($t(29)$ = -2.37, p =

0.02, two-tailed). This result suggests the presence of 'retrocochlear' disorders in the tinnitus group.
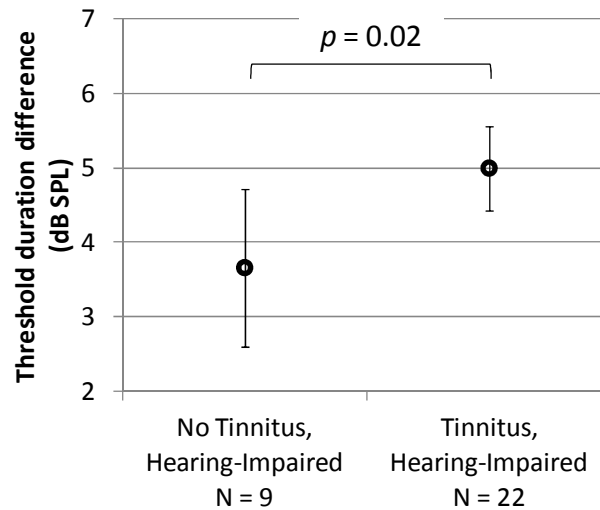
Figure 7.2: Average threshold duration differences (mean ± 95% C.I.) for hearing-impaired listeners without tinnitus and hearing-impaired listeners with tinnitus.

7.2   Average threshold duration difference at different frequencies

Average threshold duration differences were plotted at different frequencies (Figure 7.3) to investigate the trend across frequency. A linear regression line was used to estimate the slope of the threshold duration differences across frequency and then compared between the two groups. The tinnitus group had steeper slope (b = -0.61) compared to the no tinnitus group (b = -0.16). The trend across frequency was found to be significantly different between the two groups ($t(193)$ = 2.97, p = 0.003, two-tailed). The analyses in this section suggest that the threshold duration differences decreased more rapidly across frequency in the tinnitus group, than the no tinnitus group.
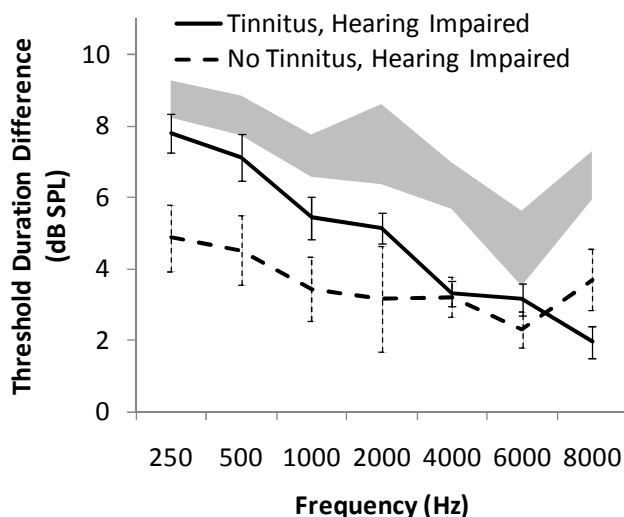
Figure 7.3: Average threshold duration differences (mean ± 1 s.e.m) at different frequencies for hearing-impaired listeners with tinnitus (solid line) and hearing-impaired listeners without tinnitus (dashed line) group. The grey area represents the average threshold duration difference (mean ± 1 s.e.m) for the normal-hearing group.

Table 7.1: Statistical p values of group differences for average threshold duration differences at each frequency bin. Criteria for significance is at p = 0.05/7 = 0.0071.

Group differences	250	500	1000	2000	4000	6000	8000
p-value (2-tailed)	0.0080	0.0357	0.0809	0.0983	0.8677	0.4494	0.0819

Table 7.1 describes exploratory analyses to investigate group differences at each

frequency bin. Readjustments for multiple comparisons were carried out using Bonferroni

correction, with the new criteria for significance at p = 0.0071.

7.3   Discussion

Threshold duration differences have been suggested as a diagnostic tool to differentiate

between 'cochlear' and 'retrocochlear' pathologies. However, previous attempts at this were

grossly affected by the assumptions made about Ménière's Disease as a purely 'cochlear'

problem. Threshold duration differences have never been compared between hearing-impaired

individuals, with or without tinnitus, until now. The 'cochlear' and 'retrocochlear' groups were

redefined, based on Kiang et al.'s (1970) suggested implication of the auditory nerve in people with tinnitus. The reduction in spontaneous activity in the auditory nerve is assumed to implicate the inner, and not the outer hair cells (Dallos and Harris, 1978; Wang et al., 1997). However, outer hair cells have also been purported to trigger the perception of tinnitus (Section 2.1.3). The exact contribution of these two hair cell systems to the percept of tinnitus is still unknown. 'Cochlear' dysfunction was redefined in this study to as reduced outer hair cell function while 'retrocochlear' dysfunction suggested reduced inner hair cell function.

The tinnitus group had significantly larger threshold differences, which supported the prediction of 'retrocochlear' pathology and the involvement of inner hair cell dysfunction. However, the disparity between the two hearing-impaired groups was not consistent across frequency. The tinnitus group exhibited a striking decrease of the threshold duration differences towards the high frequencies. This observation could be explained if the tinnitus group had significantly better absolute thresholds at the lower frequencies. However, no significant differences were found between the two hearing-impaired groups (Chapter 5). It is possible that the threshold duration difference is not as effective at differentiating between pathologies at higher frequencies. Plomp and Bouman (1959), for instance, also reported that threshold duration differences decreased with increasing frequency.

7.4   Conclusions

The results of this chapter suggest inner hair cell involvement in tinnitus. However, it is not possible to extend this hypothesis to frequency regions where tinnitus was generally perceived (between 4000 to 8000 Hz) because of the overlap between the two hearing-impaired groups in that region. Further analyses on the other measures of outer hair cell behaviour (frequency selectivity and compression) will be made in subsequent chapters.

Chapter 8
'Dead regions' and off-frequency shifts

Off-frequency shifts occur when the tip of the Iso-Forward Masking Contour (IFMC), detailed in Section 3.4.2, is at a different frequency from the probe frequency tested. Off-frequency shifts have been used to indicate the presence of inner hair cell damage, termed 'dead regions' (Kluk and Moore, 2006; Moore, 2004a; Moore et al., 2000). In a psychophysical tuning curve measurement, the *minimum masked frequency* (MMF) is always located at the probe frequency tested. In the presence of inner hair cell damage, however, Moore (2000) proposes that the tip may be shifted away from the probe frequency. The tip is expected to fall at the boundary of the 'dead region'. Kluk and Moore (2006) compared the ability of both simultaneous- and forward-masking methods in the detection of these 'dead regions'. They concluded that both methods produced similar results, although they preferred the simultaneous-masking method because it was supposedly easier to implement.

Another method of detecting 'dead regions' is with the use of a Threshold Equalising Noise (TEN) test (Moore et al., 2000). Weisz et al. (2006) investigated the occurrence of these 'dead regions' in normal-hearing people with tinnitus, using two methods; the TEN test and a pitch-scaling task. The TEN test suggested the presence of 'dead regions' at frequencies that were rated to be highly similar to the percept of tinnitus. The pitch-scaling task showed that tinnitus sufferers matched high-frequency tones to a lower-frequency tone, which suggested that tinnitus sufferers perceived the tones presented at a different frequency (off-frequency listening).

The TEN test is not used in this study because of the complex nature of testing hearing-impaired listeners who have tinnitus. The TEN test is also limited up to 4 kHz whereas the perception of tinnitus may be present at much higher frequencies. The presence of off-frequency listening has not been investigated in people with tinnitus. In this chapter, therefore, off-frequency shifts found in people who have tinnitus and those who do not have tinnitus will be compared. The exact contribution of inner hair cell dysfunction alone, to the percept of tinnitus, is unknown. Kiang et al. (1970), for instance, suggested abnormal spontaneous activity in the auditory nerve as a trigger for tinnitus, which suggests the presence of inner hair cell defect (Dallos and Harris, 1978; Wang et al., 1997). However, other studies suggest outer hair cell dysfunction as the trigger of tinnitus instead (Jastreboff, 1990; Shiomi et al., 1997).

The first stage in the analyses is to define the boundary for 'normal' amounts of off-frequency shifts. In Moore's (2000) original proposal, abnormal amount of off-frequency listening were defined as shifts that were 'well away' from the signal frequency, but the actual amount of shift was not clearly quantified. Therefore, a 'normal' boundary was defined in this chapter to address this issue. The next analysis involved off-frequency shift comparisons between the tinnitus and no tinnitus group; (1) averaged across groups and (2) averaged across individual frequencies. Lastly, the relationship between off-frequency shifts and the Tinnitus Spectrum was investigated. Off-frequency shifts were analysed at probe frequencies 250, 500, 1000, 2000, 4000, 6000 and 8000 Hz. A non-parametric test (Mann-Whitney) was used to compare the amount of off-frequency listening present in the two hearing-impaired groups. Quantification of off-frequency shifts are detailed in the next section.

8.1   Off-frequency shifts
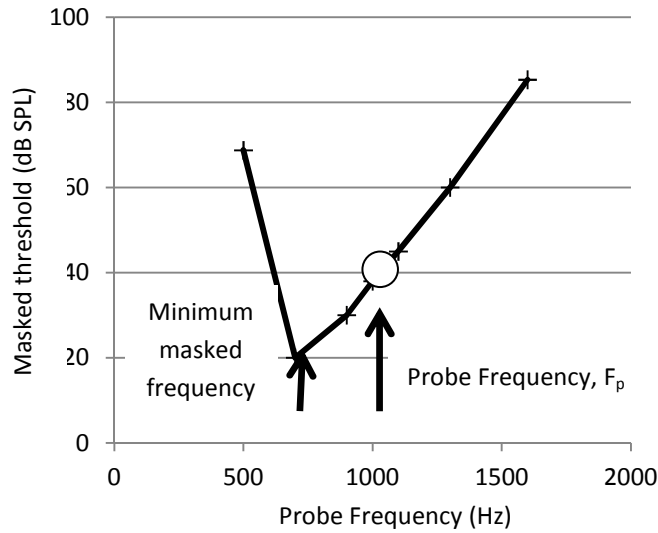
Figure 8.1: Schematic of an IFMC displaying off-frequency shift towards the low frequency.

Off-frequency listening is described as the masked frequency at which the probe tone requires the least amount of masking (Figure 8.1). This corresponds to the minimum point on the IFMC (Section 3.4.2). The presence of off-frequency listening has been attributed to inner hair cell (IHC) damage, on the assumption that outer hair cells are already damaged (Hawkins, 1973; Moore, 2004a; Moore and Alcantara, 2001). In order to quantify the amount of off-frequency listening that occurred at a particular probe frequency (F_p), the minimum point on the IFMC was first located. The amount of absolute shift from the probe frequency was calculated by finding the difference between the minimum masked frequency and the probe frequency. This was then expressed as a percentage of the probe frequency measured (see equation 1).

$$\textbf{Shift } (\%) = \frac{\textbf{(Minimum masked frequency} - \textbf{Fp)}}{\textbf{Fp}} \textbf{x 100} \qquad (1)$$

Some hearing-impaired participants presented with diagonally shaped IFMCs. These meant that it was not possible to identify the exact tip of the curve because it was beyond the bounds of the curve measured. These were represented by large shifts of 50% or 60%, which can be visually identified by the presence of a tip of the IFMC, at masker/probe frequency ratios of 0.5 or 1.6.

8.2   'Normal' amounts of shifts

The pattern of off-frequency shifts in normal-hearing is depicted in Figure 8.2. Minimal amounts of off-frequency shifts were apparent around 250 Hz and 8000 Hz. These can be attributed to the 'bowled-shaped' absolute threshold function that was measured in a previous chapter (see Figure 5.1). Absolute threshold values in the normal-hearing group are lower in the mid-frequency region (500 Hz to 4000 Hz). This means that the probe frequency in the IFMC task may be preferentially masked by an adjacent frequency that has a lower absolute threshold value. On average, the off-frequency shifts at 250 Hz and 8000 Hz can be explained by the decrease in absolute thresholds at adjacent frequencies.

The normal-hearing groups had greater variations of off-frequency shifts at the lowest frequency of 250 Hz (Figure 8.2). The upper bounds of 'normal' amounts of off-frequency shifts were defined to be within ±10% of the probe frequency. These were based on visual observations of the hearing profiles (Figure 8.3), and the variations about the median. Off-frequency shifts that were *more* than ± 10% away from the probe frequency (masker/probe frequency ratios of 0.9 and 1.1) were considered to be abnormal and were used to infer the presence of peripheral damage around the probe frequency.
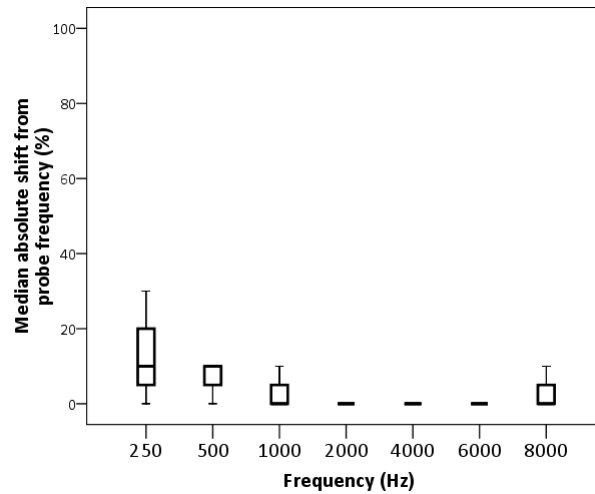
Figure 8.2: Average absolute off-frequency shifts in the normal-hearing group at different frequencies (median ± interquartile range).

These minor off-frequency shifts are also sometimes seen in the mid-frequency region. Subjects BCR_R (at 1000 Hz) and INE_L (at 2000 Hz) (reprinted in Figure 8.3) for instance, displayed small shifts at probe frequencies with normal thresholds. When absolute thresholds were re-measured at the frequencies where the tips appeared, they were found to be lower than that measured at the probe frequency. This suggests selective listening at an adjacent site in the cochlea that is more responsive to the probe frequency tested, or a representation of the threshold microstructure (Cohen, 1982). In both cases (BCR_R and INE_L), the absolute thresholds were within normal limits.
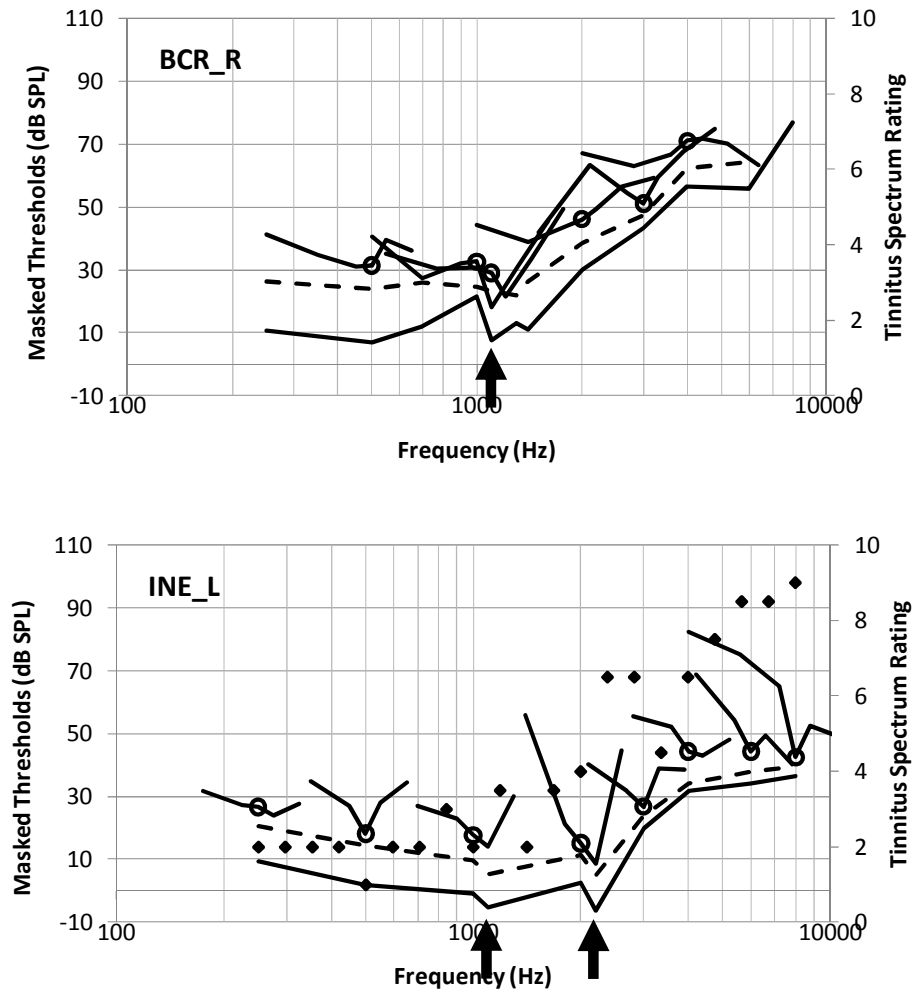
Figure 8.3: Examples of off-frequency shifts occurring at normal absolute thresholds for hearing-impaired listeners BCR_R (without tinnitus) and INE_L (with tinnitus). Black arrows indicate absolute threshold values within the normal-hearing range that coincide with off-frequency tips of the IFMC.

8.3   Average off-frequency shifts between groups

This section compares absolute off-frequency shifts in the tinnitus and no tinnitus group. Absolute off-frequency shifts were averaged across probe frequencies of 250, 500, 1000, 2000, 4000, 6000 and 8000 Hz (Figure 8.4). The median shift of the tinnitus group (8%) was within to the upper bounds of 'normal' shifts, set at ±10% in the previous section. The no tinnitus group, however, had a median shift of 18.3%. The difference between the mean score

between the two groups was 10.3%. This difference was found to be significantly different ($z = -3.80$, $p = 0.0001$, two-tailed).
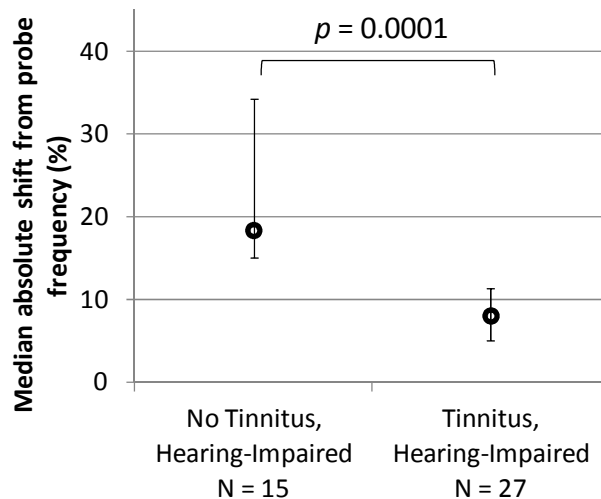
Figure 8.4: Average absolute off-frequency shifts (median ± interquartile range) for hearing-impaired listeners without tinnitus and hearing-impaired listeners with tinnitus.

The results were consistent with visual observations of a larger proportion of diagonal or shifted IFMC tips in the no tinnitus group. The tinnitus group had only minimal amounts of off-frequency shifts. On first glance, the results of this section suggest the possibility of inner hair cell dysfunction in the no tinnitus group. The implications and interpretations of these results will be discussed later in this chapter.

8.4   Average shifts at different frequencies

Figure 8.5 shows exploratory comparisons made between the median off-frequency shifts at different probe frequencies in both hearing-impaired groups. The no tinnitus group was found to exhibit consistently greater amounts of off-frequency shifts at each frequency,

compared to the tinnitus group. Group differences at each frequency bin, however, were not statistically significant (Table 8.1).
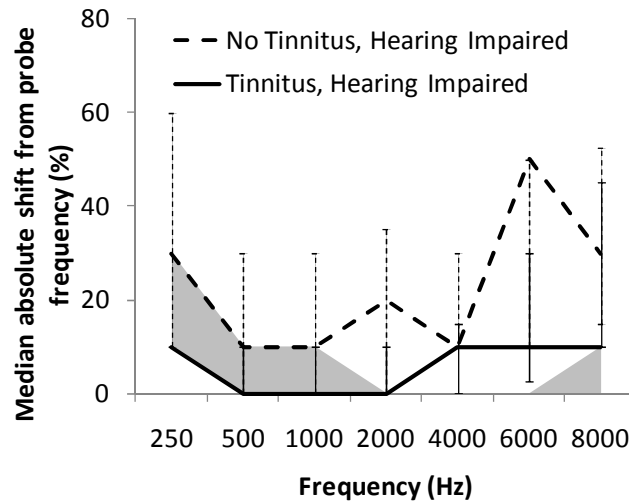
Figure 8.5: Average absolute off-frequency shift comparisons at different frequencies (median ± interquartile range), for hearing-impaired listeners with tinnitus (solid line) and hearing-impaired listeners without tinnitus (dashed line). The grey area represents the average absolute off-frequency shift (median ± interquartile range) for the normal-hearing group.

Table 8.1: Statistical p values of group differences for average absolute off-frequency shifts at each frequency bin. Criteria for significance is at p = 0.05/7 = 0.0071.

Group differences	250	500	1000	2000	4000	6000	8000
p-value (2-tailed)	0.0925	0.0145	0.0048	0.0269	0.0989	0.0691	0.2523

There was a stronger presence of off-frequency shifts in the tinnitus group compared to the group without tinnitus. This observation contradicts the prediction of a relationship between 'dead regions' and the presence of off-frequency shifts in people who have tinnitus. The greater presence of off-frequency shifts in the no tinnitus group suggests the possibility of a differentiation in terms of cochlear pathology.

8.5 Tinnitus Spectrum and Off-frequency Shifts

Figure 8.6 shows the maximum ratings on the Tinnitus Spectrum as a function of off-frequency shifts in the tinnitus group. The results observed indicated that most of the participants rated pure tones of frequencies between 4000 to 8000 Hz to be most similar to the percept of tinnitus. This frequency region coincided with an increase in off-frequency shifts. Unfortunately, it is not possible to speculate a direct relationship between the two variables because the no tinnitus group also had increasing off-frequency shifts in the same frequency region. Comparisons between off-frequency shifts between the normal-hearing group and the hearing-impaired group with tinnitus, on first glance, suggest some form of impairment present. However, the off-frequency shifts in hearing-impaired listeners here could be a consequence of by their steeply-sloping thresholds in the same frequency region, and may not be indicative of damage per se.
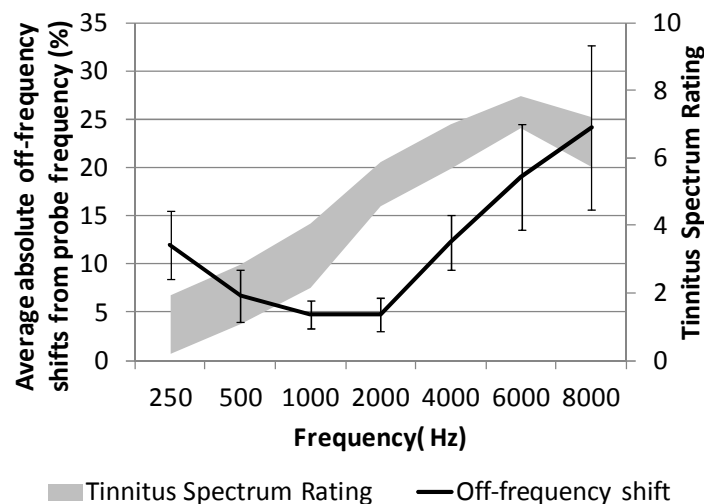
Figure 8.6: Average absolute off-frequency shifts at different frequencies (solid line, right axis) for hearing-impaired listeners with tinnitus (median and inter quartile range shown). The average maximum rating on the Tinnitus Spectrum task (mean ± 95% C.I., left axis) is shown as the greyed area.

8.6   Discussion

A more prevalent presence of off-frequency shifts was found in hearing-impaired people *without* tinnitus. Off-frequency shifts have been suggested to indicate the presence of inner hair cell damage (Moore, 2004a; Moore and Alcantara, 2001). Although inner hair cell function has been investigated in people with tinnitus using the Threshold Equalising Noise method (Weisz et al., 2006), the exclusive use of off-frequency shift analyses has not been explored. The analyses in previous chapters of this thesis provided support for the possibility of inner hair cell damage in people with tinnitus. This would predict a greater presence of off-frequency shifts in people with tinnitus. However, the analyses in this chapter have been contradictory; people *without* tinnitus showed a *greater* prevalence of off-frequency shifts (greatest at 500 Hz and 6000 Hz) while people with tinnitus had minimal amounts of shifts that were similar to that seen in normal-hearing listeners.

These observations have to be explained in the context of the assumptions made about off-frequency shifts and its relationship to presumed inner hair cell damage. The relationship between the two parameters was based on two assumptions; (1) outer hair cell damage precedes inner hair cell damage (Hawkins, 1973; Nordmann et al., 2000), and (2) off-frequency shifts were found in animals with induced outer hair cell damage (Liberman and Dodds, 1984). Based on these physiological evidence of animal studies, Moore (2004a) suggested that the tuning of the basilar membrane will be impaired in people who showed signs of inner hair cell damage, even over regions that do not sustain such damage. This means that off-frequency shifts should be interpreted as outer hair cell damage with the possibility that the inner hair cells have also been affected. The logic behind the explanation of the off-frequency shifts, therefore, suggests that the tinnitus group has minimal outer hair cell damage at the lower

frequencies. At higher frequencies, however, the tinnitus group may have more extensive outer

hair cell damage, but this is comparatively less than the no tinnitus group.

The presence of functional outer hair cell behaviour existing in conjunction with

impaired inner hair cell function contradicts the assumption that outer hair cells are *more*

vulnerable than inner hair cells. However, recent studies by Kujawa and Liberman (2006, 2009)

have provided supporting evidence for the possibility that outer hair cells may not be the first

site of damage in noise trauma. They observed normal outer hair cells in the presence of

abnormal inner hair cell activity. They also reported the occurrence of neural degradation that

happen post noise trauma caused by dysfunction of the synaptic ribbons at the base of the

inner hair cells. The main differences between the Kujawa and Liberman's (2006, 2009) studies

and physiological studies done on noise exposed animals in the past, lie in the levels of the

traumatising stimuli used. Earlier studies used traumatising noise stimuli which were in excess

of 100 dB SPL, while Kujawa and Liberman (2006, 2009) exposed their animal subjects to

sounds that were about 100 dB SPL (moderately loud). Although the use of loud, traumatising

stimuli causes extensive cochlear damage, it may not always represent the damage experienced

by human subjects who are able to choose to protect themselves from the offending sound

(Saunders et al., 1985; Schmiedt, 1984). This means that the outer hair cells may not be the

primary point of insult that is suffered by most people.

The debate over the primary point of insult in a damaged cochlea makes 'dead regions'

very difficult to decipher. This is because the depicted shift can now be interpreted in terms of

outer hair cell damage, or preferential listening at adjacent frequencies, due to inner hair cell

dysfunction. The actual amount of cochlear damage that would contribute to the presence of

shifts is unknown. However, the difference in amounts of shifts across frequency, in the tinnitus

group, provides some support for Kiang et al.'s (1970) interpretation of the 'Edge Effect' theory that assumes disparity between 'normal' and 'abnormal' regions.

Comparison between the off-frequency shifts and the Tinnitus Spectrum suggested that the tinnitus percept could be related to increasing off-frequency shifts in the tinnitus group. This could be perceived as some form of damage to the periphery. However, it is not possible to speculate on the type of damage present because greater increase in off-frequency shifts was found in the no tinnitus group.

8.7   Conclusions

1.   The tinnitus group had comparatively less off-frequency shifts across frequency, compared to the no tinnitus group. The tinnitus group had 'normal' shifts up to 1000 Hz, with a gradual increase in shifts towards the higher frequencies.

2.   The interpretations of 'dead regions' propose a greater amount of outer hair cell damage in the group without tinnitus.

3.   The gradual increase in off-frequency shifts in the tinnitus group coincided with frequency regions where tinnitus was perceived on the Tinnitus Spectrum. However, this may be a consequence of steeply-sloping absolute thresholds at the frequency region and not due to damage per se.

Chapter 9
Frequency Selectivity

This chapter compares the differences in frequency selectivity, or the ability to detect a tone in the presence of competing tones, between hearing-impaired listeners with tinnitus and hearing-impaired listeners without tinnitus. Frequency selectivity, measured using IFMCs detailed in Section 3.4.2, is believed to rely on good outer hair cell function (Evans, 1975; Ryan et al., 1979). Outer hair cell impairment has been suggested to be worse in people with tinnitus, compared to those with similarly impaired hearing but without tinnitus (Jastreboff, 1990). Jastreboff's discordant theory proposes that more extensive damage in the outer hair cell system results in disinhibition at the dorsal cochlear nucleus, and the hyperactivity that emerges from the condition is interpreted by the brain as sound. Implications of outer hair cell damage in tinnitus studies have been made by investigating DPOAE responses (Janssen et al., 1998; Ozimek et al., 2006; Shiomi et al., 1997) and psychoacoustical measures (Mitchell and Creedon, 1995). These studies were performed on tinnitus sufferers with normal-hearing, and compared with normal-hearing but without tinnitus. However, similar comparisons have not been previously made on people with hearing-impairment, and will be investigated in this chapter. Frequency selectivity is measured with the use of a forward-masking paradigm (Section 3.4.2). It is then quantified in this chapter using Q_{10} values.

It has to be emphasised at this point, that Q_{10} values are traditionally used to estimate the amount of neural tuning present in the auditory nerve. This is not synonymous to the way Q_{10} values are interpreted in this chapter, because psychophysical measurements of frequency selectivity are not the same as measuring neural tuning curves from the auditory nerve. This is

because, as with most psychophysical measurements, the contribution of complex central processes cannot be completely excluded. However, similar assumptions can be applied. High Q_{10} values would indicate good frequency selectivity, while low Q_{10} values suggest poorer frequency selectivity.

Firstly, the quantification of frequency selectivity is explained in detail. This is followed by comparisons (1) between groups and (2) across individual frequencies. Measures of frequency selectivity have been shown to be reliant on the level of the probe used (Nelson and Freyman, 1984), and the consequence of this will be explored in (3) normal-hearing individuals and (4) compared against those with tinnitus. Some participants exhibited abnormally shaped IFMCs (for instance, diagonal lines), where it was impossible to estimate the Q_{10} values. Comparison of the Q_{10} mean values was carried out using an independent t-test for the two hearing-impaired groups.

9.1 Q_{10} Values

The Iso-Forward Masking Contours (IFMCs) measured in this study are an estimate of the amount of frequency selectivity present. The masker frequencies were set at masker/probe frequency ratios of 0.5, 0.7, 0.9, 1, 1.1, 1.3 and 1.6, and were measured across different probe frequencies (Section 3.4.2). The Q_{10} quantification method was used to quantify the gross differences present between the two hearing-impaired groups. In this study, the Q_{10} values should not be interpreted as the conventional measure of the broadness of 'neural auditory filters', rather, it is a value that estimates the amount of frequency selectivity that is present.

The slopes of the best fit lines that passed through the minimum masked frequency on the IFMC were estimated for the Q_{10} calculations. The frequency bandwidth between the two slopes that are 10 dB above the minimum masked frequency, were calculated and the Q_{10} value

obtained. The Q_{10} values were calculated by dividing the minimum masked frequency (MMF),

or the minimum point of the IFMC, by the bandwidth that is 10 dB above the minimum masked

frequency (see the equation (2) below and Figure 9.1).

$$Q_{10} \text{ value} = \frac{\textbf{Minimum masked frequency}}{\textbf{Bandwidth}_{(10\text{ dB})}} \qquad (2)$$
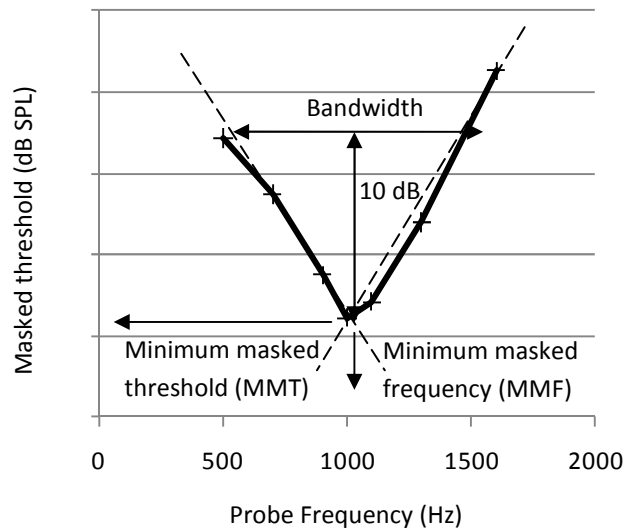
Figure 9.1: Schematic of Q_{10} calculation used to quantify the amount of frequency selectivity present.

A higher Q_{10} value describes a sharper V-shaped curve (better frequency selectivity),

whereas a lower Q_{10} value describes a broader U-shaped curve (poorer frequency selectivity).

The calculation of Q_{10} values was not possible in the presence of a complete collapse of the

IFMC. This is, for instance, if the minimum masked frequency occurred at the extreme ends of

the IFMC and formed a diagonal line. IFMCs shaped this way were excluded from the Q_{10}

analysis.

9.2 Average Q_{10} values between groups

This section compares the average Q_{10} values between hearing-impaired listeners with tinnitus and hearing-impaired listeners without tinnitus. Q_{10} values were averaged across probe frequencies of 250, 500, 1000, 2000, 4000, 6000 and 8000 Hz (Figure 9.2). The mean Q_{10} value for the hearing-impaired listeners with tinnitus was 2.15, and the mean Q_{10} value for the hearing-impaired listeners without tinnitus was 1.39. The difference between the mean Q_{10} values was 0.76. This was found to be significantly different between the two groups ($t(38) = -2.61$, $p = 0.013$, two-tailed). The lower Q_{10} value in the no tinnitus group suggests the presence of damaged outer hair cell function.
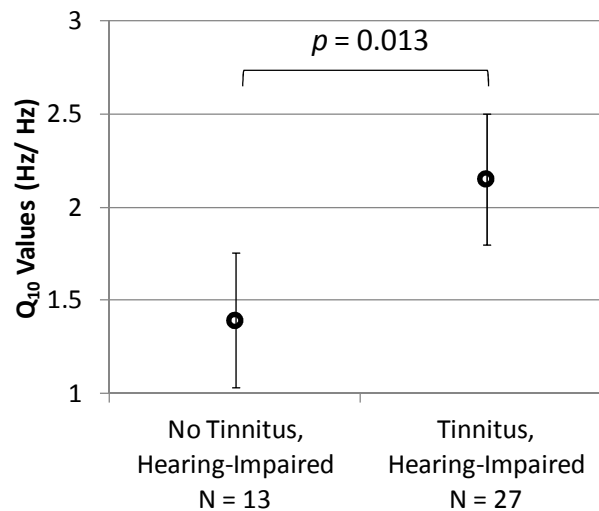
Figure 9.2: Average Q_{10} values (mean ± 95% C.I.) for the no tinnitus and tinnitus group.

9.3 Average Q_{10} values at different frequencies

This section investigates the trend of the Q_{10} values at different probe frequencies in both hearing-impaired groups (Figure 9.3). The tinnitus group had consistently higher Q_{10} values compared to the no tinnitus group across frequency, which included the frequency region where tinnitus was perceived. The Q_{10} comparison suggests the possibility that the no

tinnitus group suffers from greater outer hair cell damage. This contradicts the prediction of the

discordant theory that would assume more extensive outer hair cell damage in the tinnitus

group (Jastreboff, 1990).
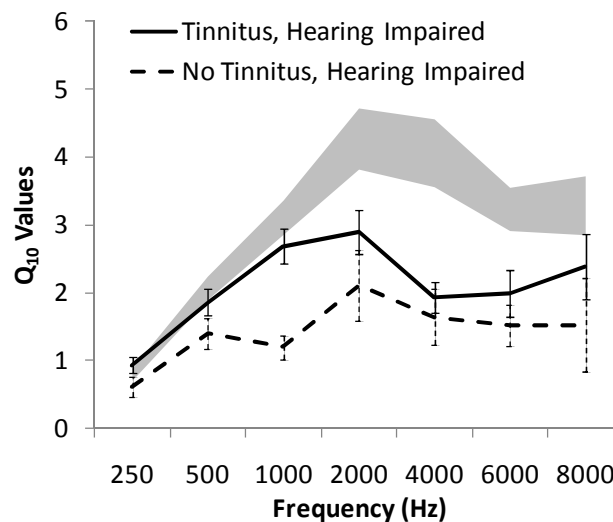
Figure 9.3: Average Q_{10} values at different frequencies (mean ± 1 s.e.m), for hearing-impaired listeners with tinnitus (solid line) and hearing-impaired listeners without tinnitus (dashed line). The grey area represents average Q_{10} values (mean ± 1 s.e.m) for the normal-hearing group.

Table 9.1: Statistical p values of group differences for average Q_{10} values at each frequency bin. Criteria for significance is at p = 0.05/7 = 0.0071.

Group differences	250	500	1000	2000	4000	6000	8000
p-value (2-tailed)	0.1168	0.1506	**0.0000**	0.2262	0.5053	0.5827	0.3737

Table 9.1 describes exploratory analyses to investigate group differences at each

frequency bin. Readjustments for multiple comparisons were carried out using Bonferroni

correction, with the new criteria for significance at *p* = 0.0071.

9.4 Q_{10} Values at high probe levels

The analyses in the previous sections showed that the hearing-impaired groups had

broader forward-masking curves compared to the normal-hearing group. This broadening could

be caused by outer hair cell dysfunction, which would result in impaired frequency selectivity. However, an alternative explanation is provided by Nelson and Freyman (1984) who reported broadening of forward-masking curves when measured at high probe levels in normal-hearing listeners. This meant the broad forward-masking curves measured by the IFMC method in the hearing-impaired groups could partly be accounted for by the higher probe levels used.

Forward-masking curves were retested in normal-hearing listeners, using the IFMC method to confirm that the effect was as observed by Nelson and Freyman (1984). Two participants (CTA and MPA) were tested at the same probe intensity as the hearing-impaired groups. The mean probe intensity for the tinnitus group was at 52 ± 19 dB SPL, while the mean probe intensity for the no tinnitus group was at 59 ± 17 dB SPL. The normal-hearing participants were tested at 10 dB SPL intervals around the higher of the two probe intensities (59 dB SPL). The higher of the two probe intensities would reflect the worst-case broadening of the forward-masking curves. The normal-hearing participants were tested at 250, 1000 and 6000 Hz at probe levels of 29, 39, 49, 59 and 69 dB SPL.

Testing at further higher levels was not comfortable to the participants and was, therefore, not pursued. Probe intensities that were below the absolute thresholds of the normal-hearing participants meant that the IFMC task could not be completed (probe tone could not be heard), and were omitted in such instances.

The results of the IFMCs tested at high probe levels in normal-hearing adults are as shown in Figure 9.4. The results showed that broadening is minimal with increasing probe level at lower frequencies, but increases at higher frequencies. Nelson and Freyman (1984) explains this broadening at higher probe levels as a consequence of nonlinearity that affects the behaviour of the forward-masking tasks. Higher masker levels are required to mask the high

probe level. The broader spread of excitation pattern resulting from higher masker levels

consequently acts as a more effective masker than when at lower masker levels.

A) IFMCs with increasing probe level

B) Q_{10} values with increasing probe level
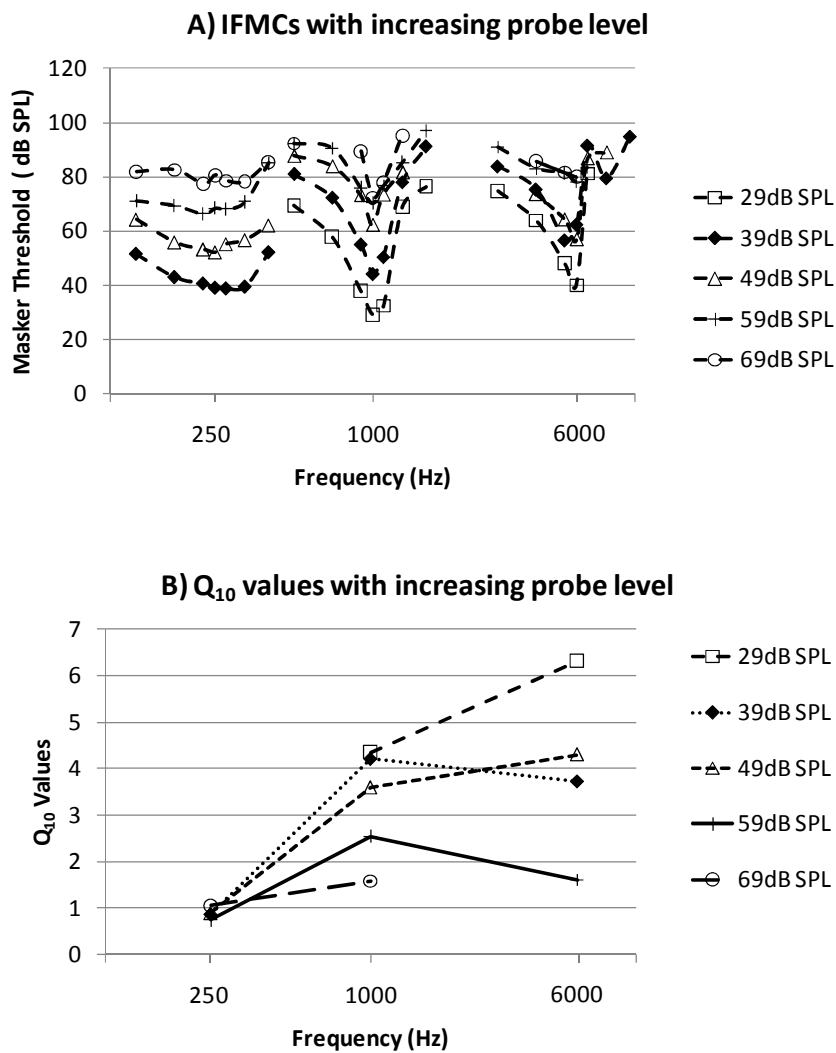
Figure 9.4: (A) Average IFMCs for normal-hearing listeners at different probe level across 250 Hz, 1000 Hz and 6000 Hz (29 dB (open square), 39 dB (filled diamond), 49 dB (open triangle), 59 dB (cross) and 69 dB (open circle)). (B) Average Q10 values for normal-hearing listeners at the same probe frequencies and probe levels as in (A).
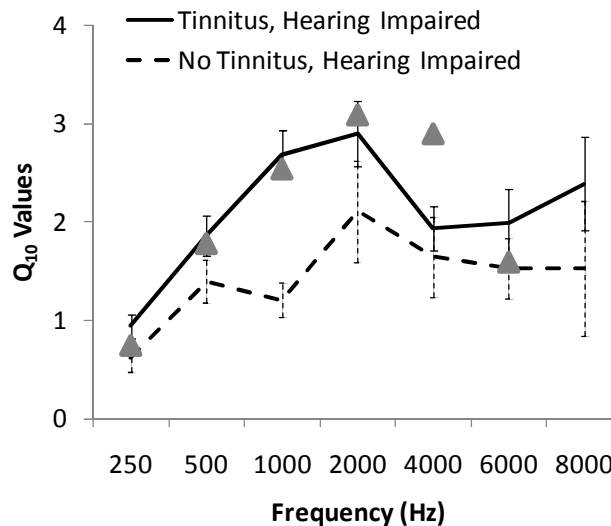
Figure 9.5: Average Q_{10} values (mean ±1 s.e.m) for hearing-impaired listeners with tinnitus (solid line) and hearing-impaired listeners without tinnitus (dashed line). The grey triangles represent average Q_{10} values (mean ±1 s.e.m) for normal-hearing listeners that were measured with a probe level of 59 dB SPL.

The results show that the reduction in Q_{10} values (at higher probe levels) in the tinnitus group can be partially explained by the fact that the IFMCs were tested at high probe levels (Figure 9.5). This suggests the Q_{10} values for some participants with tinnitus may even be *comparable* to those of a normal-hearing person when tested at high probe levels, especially between 250 to 2000 Hz. The Q_{10} values of the no tinnitus group, on the other hand, were much lower than the Q_{10} values of normal-hearing people tested at high probe levels.

9.5   Discussion

Frequency selectivity was measured to infer outer hair cell behaviour. The presence of good frequency selectivity was represented by high Q_{10} values, while low Q_{10} values suggested poorer frequency selectivity. The hearing-impaired groups both depicted lower Q_{10} values compared to the normal-hearing group. This was consistent with other reported observations of reduced frequency selectivity in the presence of hearing impairment (Evans, 1975; Ryan et

al., 1979). Surprisingly, however, frequency selectivity was observed to be better in people with tinnitus compared to those without tinnitus. This contradicted the hypothesis proposed by the discordant theory that would assume comparatively worse outer hair cell dysfunction in people with tinnitus (Jastreboff, 1990). The reduction of the Q_{10} values in the hearing-impaired groups could be explained by (1) reduced outer hair cell function, and by (2) testing at high probe levels, as proposed by Nelson and Freyman (1984).

Nelson and Freyman (1984) first reported that forward-masking curves, tested on people with normal-hearing, broadened when tested at high probe levels. This provided an alternative explanation to the reduction in Q_{10} values in the hearing-impaired groups, because they were mostly tested at high probe levels. For this reason, the effect was simulated in this chapter, to quantify the effect of using high probe levels on the task. Normal-hearing individuals were tested at a similarly intense probe level (59 dB SPL) to that used for the hearing-impaired group. The results obtained were consistent with the observations made by Nelson and Freyman (1984); distinct broadening of the IFMCs was evident at high probe levels. The Q_{10} values that were measured at high probe levels in normal-hearing listeners were then compared against the tinnitus group, where evidence of overlap was present. This indicated that some of the lower Q_{10} values (broader IFMC curves) observed in the hearing-impaired groups may be accounted for by the use of high probe levels. In fact, it is possible to speculate that the tinnitus group may have relatively *normal* frequency selectivity at those frequencies. The no tinnitus group, on the other hand, had comparatively worse Q_{10} values and it is highly likely that their reduction in frequency selectivity is also affected by damage to cochlear function.

9.6   Conclusions

1.   The IFMCs measured in people with tinnitus were significantly sharper than those measured in people without tinnitus, suggesting that people with tinnitus have *better* frequency selectivity, and possibly *better* outer hair cell function. People who have damaged hearing but no tinnitus, on the other hand, were observed to have poorer frequency selectivity.

2.   A proportion of people with tinnitus in this study have frequency selectivity that may be comparable to that measured in normal-hearing people at high probe levels.

Chapter 10
Compression

Compression is believed to be a consequence of the nonlinear behaviour of the inner ear whereby an increase of sound levels results in a disproportionate increase of vibration at the level of the basilar membrane (see Sections 2.5 and 3.4.3). This nonlinear behaviour of the inner ear allows humans to have a wider dynamic range of hearing, and a greater tolerance to loud sounds. The compression coefficient of compression is estimated to be between 0.2 and 0.3, which is an indication of the amount of compression applied by the inner ear. The compressive region is believed to be between 30 to 40 dB SPL, and 80 dB SPL. The inner ear behaves linearly, beyond the compressive region (see Figure 10.1).
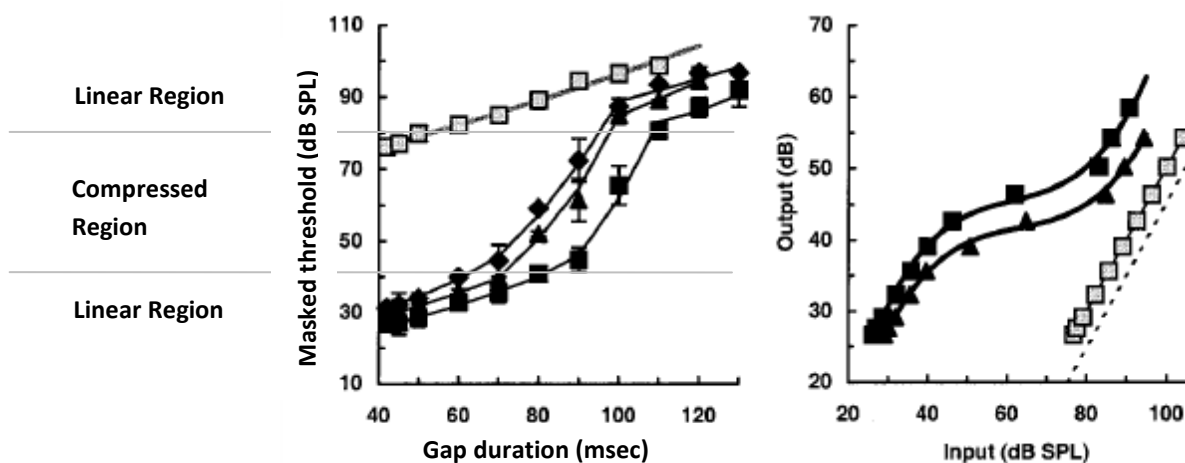
Figure 10.1: Schematic of normal-hearing Temporal Masking Curves (left) and the input/ output function derived from the Temporal Masking Curves (right), adapted from Nelson et al. (2001). The filled squares and triangles represent on-frequency measurements (at masker/ probe frequency of 1) and the grey squares represent off-frequency measurements (at masker/ probe frequency of 0.55).

Temporal Masking Curves (TMCs) (see Figure 10.1, left) have only recently been introduced as a new method to estimate the amount of peripheral compression (Lopez-Poveda et al., 2003; Nelson et al., 2001). These studies used a forward-masking paradigm, which measured masker thresholds at a masker/ probe frequency ratio of 1 and at a much lower masker/ probe frequency ratio of about 0.55 (see Section 3.4.3 for detailed TMC procedures carried out in this study). TMCs are typically measured with the intention of deriving the input/ output function of the basilar membrane, and require more than 10 data points to obtain a good estimate. TMC slopes were reported to be *shallower* in hearing-impaired individuals compared to normal-hearing controls, although *variations* on the amount of compression was reported *within* the hearing-impaired group (Lopez-Poveda et al., 2005). Compression is believed to be reliant on good outer hair cell function (Robles and Ruggero, 2001; Ruggero and Rich, 1991) and outer hair cell damage has been suggested to be a trigger for tinnitus (Jastreboff, 1990; Shiomi et al., 1997). However, more recent evidence suggest that outer hair cells are not as vulnerable to damage as once believed (Kujawa and Liberman, 2009; Stamataki et al., 2006). In light of new evidence, TMCs are used to investigate the relationship between outer hair cell damage and tinnitus.

TMCs will be used in this thesis to infer outer hair cell function in hearing-impaired people with tinnitus and those without tinnitus. This will be carried out using a forward-masking paradigm, but with a smaller number of measurement points (5 points). This chapter will focus on the gross difference between the two groups and will not be deriving the input/ output function from the TMC measurement, thus a small number of measurement points should be sufficient to achieve this. The slope of the TMC function will be compared with the slopes found in 'normal' TMCs. Steep TMC slopes suggest a presence of compression while shallower TMC slopes suggest an absence of compression. TMC slopes will be analysed at probe

frequencies of 250, 500, 1000, 2000, 4000, 6000 and 8000 Hz. An independent t-test will be

used to compare the mean slopes between the two hearing-impaired groups.

10.1 Deducing the presence of compression

The TMC measure consists of masker thresholds measured at different gap durations

(0.02, 0.04, 0.05, 0.06 and 0.08 s). The steepness of the function indicates the amount of

compression present at a particular frequency. Compression is quantified by fitting a straight

line to the data points to obtain the slope of the line (Figure 10.2). High TMC slope values are

consistent with the observation that compression is present (which suggests intact outer hair

cell function) while low TMC slope values suggest that there is less compression at the probe

frequency tested.
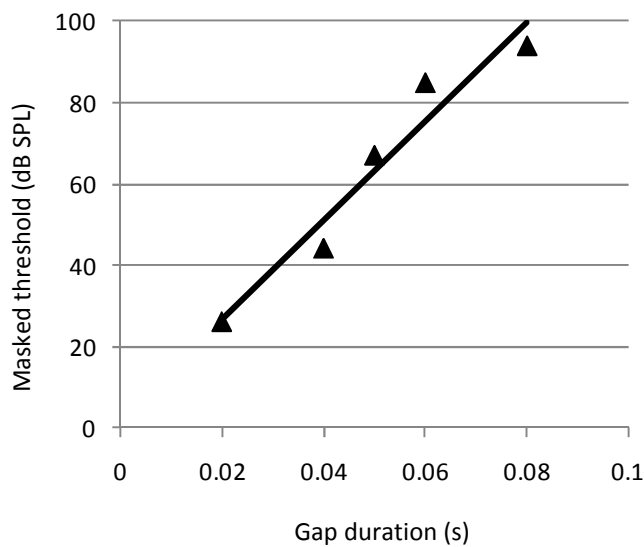
Figure 10.2: Schematic of a normal-hearing Temporal Masking Curve (filled triangles). A linear
trendline is fitted to the data points to obtain the estimate of the slope, which is an indication
of the amount of compression present.

10.2 Average compression between groups

This section compares the average TMC slopes across frequency between the tinnitus and no tinnitus group (Figure 10.3). The tinnitus group had a mean slope of 302 dB SPL/ s while the no tinnitus group had a shallower slope of 155 dB SPL/ s. The difference of 147 dB SPL/ s between the two groups was found to be significant ($t(36)$ = -2.75, p = 0.009, two-tailed). The shallower slope observed in the no tinnitus group suggests a greater extent of outer hair cell damage in this group.
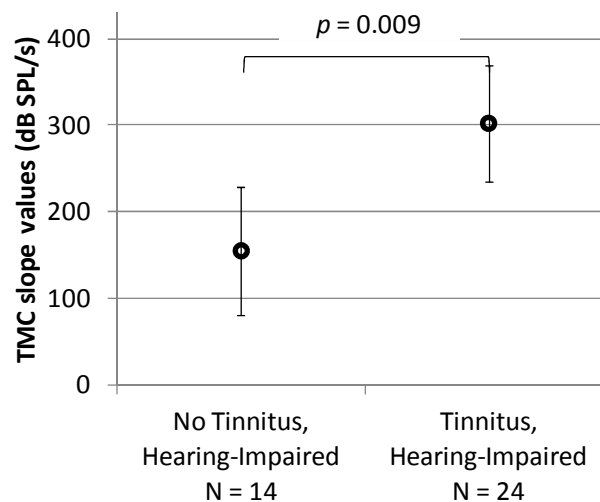
Figure 10.3: Average TMC slopes (mean ± 95% C.I.) for hearing-impaired listeners without tinnitus and hearing-impaired listeners with tinnitus.

10.3 Average compression at different frequencies

This section investigates the trend of the TMC slopes at different probe frequencies in both hearing-impaired groups (Figure 10.4). The tinnitus group was observed to have consistently higher TMC slope values, at all frequencies, compared to the no tinnitus group. This included the high-frequency region where tinnitus was perceived. The TMC slope comparison suggests the possibility that the no tinnitus group suffered from greater outer hair

cell damage compared to the tinnitus group. What is also of interest is the obvious TMC slope decrease from 1000 Hz to 8000 Hz, in the tinnitus group. The hearing-impaired group without tinnitus displayed constant TMC slope values across all frequencies.
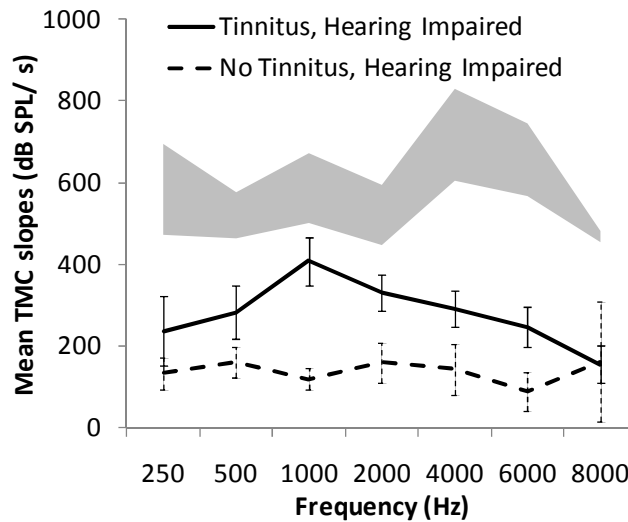
Figure 10.4: Average TMC slope values (mean ± 1 s.e.m) at different frequencies for hearing-impaired listeners with tinnitus (solid line) and hearing-impaired listeners without tinnitus (dashed line) group. The grey area represents the average TMC slope values (mean ± 1 s.e.m) for the normal-hearing group.

Table 10.1: Statistical p values of group differences for average TMC slope values at each frequency bin. Criteria for significance is at p = 0.05/7 = 0.0071.

Group differences	250	500	1000	2000	4000	6000	8000
p-value (2-tailed)	0.2958	0.1243	0.0001	0.0231	0.0635	0.0590	0.9544

Table 10.1 describes exploratory analyses to investigate group differences at each frequency bin. Readjustments for multiple comparisons were carried out using Bonferroni correction, with the new criteria for significance at $p = 0.0071$.

10.4 TMC slopes at high probe levels

Frequency selectivity analyses in the previous chapter demonstrated a broadening of the forward-masking curves as a consequence of using high probe levels, first reported by Nelson and Freyman (1984). This section investigates if a similar process might be at work with the TMC measurements because the TMC method also employs a forward-masking paradigm. Lopez-Poveda et al. (2008) compared the TMC functions at probe levels of 9 and 15 dB SL, which demonstrated steeper TMC slopes when using higher probe levels.
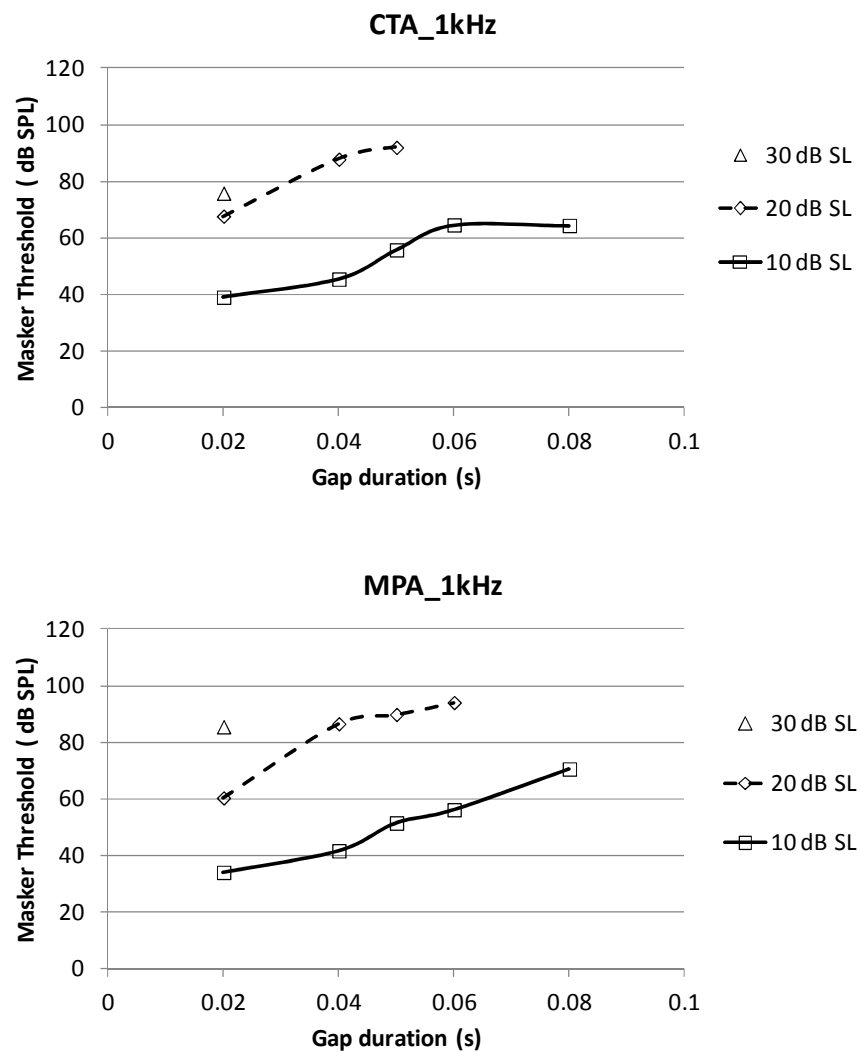
Figure 10.5: Average TMCs measurements obtained at high probe levels (10, 20 and 30 dB SL) for normal-hearing listeners.

Two normal-hearing participants were tested in this study (Figure 10.5), at various sensations levels in order to replicate the observations reported by Lopez-Poveda et al. (2008). The TMC functions were also observed to rise quicker when using higher probe levels (for gap durations 0.02 and 0.04 s). This produces an overall impression of steeper TMC slopes. It was not possible to make measurements at the same probe levels as the hearing-impaired groups because the masker level required to mask the high-level probe tones often exceeded the maximum output limit set by the program.

The steeper TMC slope at higher probe levels could explain the observations made in the hearing-impaired groups. High probe levels were often used to make the TMC measurements in the hearing-impaired groups. This means that the presence of normal compression in combination with raised thresholds would be observed as a two-portioned TMC function (quick rise in masker thresholds between 0.02 and 0.04 s, followed by a plateau). Interestingly, this pattern of TMC function was often seen in the tinnitus group, whereas the no tinnitus group displayed typically flatter TMC functions (for examples see Figure 10.6).
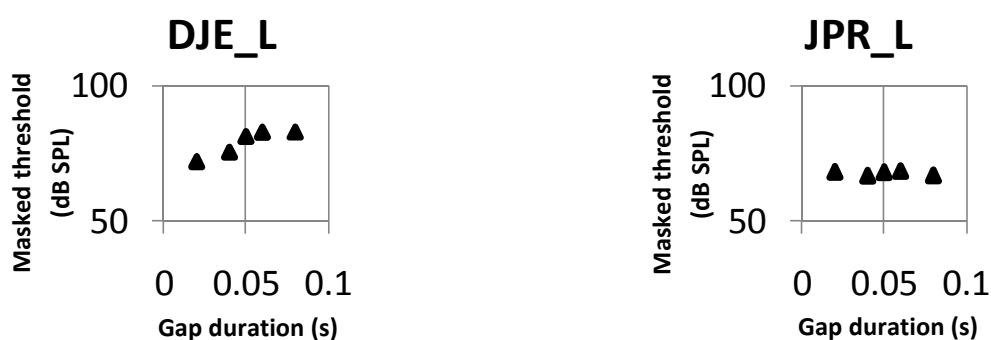
Figure 10.6: Examples of TMC functions found in a hearing-impaired listener with tinnitus (DJE_L, left panel) and in a hearing-impaired listener without tinnitus (JPR_L, right panel). TMCs were measured at 6000 Hz and at similar probe levels.

Despite the presence of a steep section in the tinnitus group, the TMC slopes values were significantly lower than the normal-hearing group. This suggests that different processes affect the slope of the TMC in the tinnitus group. This may include the loss of compression or other mechanisms that influence the rate of recovery from forward masking.

10.5 Discussion

The results of this chapter support the previous conclusion drawn on the frequency selectivity that suggested better outer hair cell function in people with tinnitus compared to those without tinnitus. TMC functions were used to infer the strength of compression, which depends on good outer hair cell function (Ruggero and Rich, 1991). Steep TMC slopes suggest a stronger presence of compression while shallower TMC slopes suggest less compression. The TMC slopes were compared between the tinnitus and no tinnitus group and the TMC slopes were observed to be *steeper* in the tinnitus group compared to the no tinnitus group. The differentiation between the TMC slopes in hearing-impaired people is consistent with previous observations by Lopez-Poveda et al. (2005), who also reported that hearing-impaired listeners with similar absolute thresholds exhibited different degrees of compression. In their study, the authors proposed that steeper TMC slopes would be observed in hearing-impaired people who have inner hair cell damage, which would not affect compression.

The TMC slopes were also measured at high probe levels in the normal-hearing group to check if they were influenced in the same way as the frequency selectivity task, because of the use of the forward-masking paradigm. The results replicated those reported by Lopez-Poveda et al. (2008), who also found steeper TMC functions with increasing probe levels. The TMC functions that were measured at high probe levels could be identified by a steep portion, up to gap duration of 0.04 s. These patterns were only observed in the tinnitus group. However, the

overall steepness of the TMC slopes in the tinnitus group was lower than that of the normal-hearing group. It is therefore not possible to conclude 'normal' amounts of compression in the tinnitus group.

10.6 Conclusions

1.   The results of the TMC slope analyses suggested significantly steeper TMC slopes in people with tinnitus compared to those without tinnitus.

2.   The pattern of the TMC slopes in the tinnitus group that were measured at high probe levels were consistent with those measured in the normal-hearing group, but at high probe levels. However, the TMC slopes were shallower in the tinnitus group compared to the normal-hearing group.

3.   The results therefore suggest that the tinnitus group may have better compression than the no tinnitus group, but it is not possible to exclude the possibility that other processes that influence the TMC function may be impaired.

Chapter 11
Uncomfortable Loudness Levels

This chapter compares the tolerance levels between the two hearing-impaired groups. The presence of recruitment or intolerance to moderately loud sounds has been thought to be linked to the loss of the compressive nonlinear behaviour, moderated by the outer hair cells (Moore and Oxenham, 1998). Recruitment is measured in terms of uncomfortable loudness levels (ULLs). This is a measure of the tolerance to increments of loud pure tones. However, ULLs have also been used to measure another audiological phenomenon called hyperacusis. Although both recruitment and hyperacusis are quantified with the same measurement method (ULLs), it is important that the distinction between these two conditions is made at this point.

Hyperacusis been reported to be present in about 40% of people with tinnitus (Goldstein and Shulman, 1996). It is also prevalent in people with normal-hearing but with genetic disorders like Williams syndrome. It refers to abnormal discomfort or startle response to environmental sounds, and has been sometimes used interchangeably with phonophobia, which may suggest psychological aversion in people with hyperacusis (Goebel and Floezinger, 2008; Goldstein and Shulman, 1996; Nigam and Samuel, 1994).

Recruitment, on the other hand, has often been investigated in people with hearing impairments, and is a description of the reduced dynamic range of hearing that is available. The hearing-impaired individual may have comparatively normal ULLs, slightly lower ULLs (believed to be caused by loss of the compressive ability of the cochlea) or higher ULLs (louder sounds are tolerated) (Moore, 2007).

ULLs are used in this thesis as a measure of recruitment and not hyperacusis. This is because hyperacusis can manifest itself as a psychological aversion, which may, or not may not be related to the presence of recruitment. The presence of recruitment, on the other hand, describes a reaction to a physical defect that can be estimated quantitatively. Recruitment is thought to be caused by impaired outer hair cell function that results in the loss of compression, which consequently makes sounds seem louder than they should be. Procedures to carry out ULL measurements were detailed in Section 3.4.4.

11.1 Minimum Uncomfortable Loudness Levels (ULLs) between groups

The level of pure tones required to afflict discomfort in each participant was examined in the analyses. These uncomfortable loudness levels (ULLs) were measured between 250 to 8000 Hz. It was not possible to obtain a numerical value for the ULL measurement if the sounds presented exceeded the maximum output limit of the soundcard. These 'extreme' values were coded at '200' to mean that the ULL at that particular frequency had a value that was above the maximum output limit of 100 dB SPL.

In the following analysis therefore, the minimum ULL was examined. This was preferred because some participants had ULLs that were above 100 dB SPL across all frequencies measured, so it was not possible to estimate a mean value from the set of data. The minimum ULL also excluded the effect of frequency. This is a desired effect of the analysis because it assumes that cochlear damage can also be present at frequencies that do not display abnormalities in the audiogram.

The ULLs were divided into three categories across the two groups; less than 90 dB SPL, between 90 to 100 dB SPL and more than 100 dB SPL (Figure 11.1). This was done to account

for the presence of non-measurable ULLs that were above 100 dB SPL, and to investigate if there was a trend of increasing tolerance to loud sounds between the two groups.

A two-sample statistical rank test for frequency tables was used to investigate the relationship between the two hearing-impaired groups across the three ULL categories with increasing loudness levels (Meddis, 1984). This is an adaptation of the Wilcoxon and Mann-Whitney tests, which allow for the analysis of data presented in the form of frequency tables. Demonstrably *lower* ULL results (thus lower tolerances to loud sounds) would suggest the presence of possible outer hair cell damage. Overall, the results suggest that the group without tinnitus has a lower tolerance to loud sounds. However, the difference between the two groups were not found to be statistically significant (z = -1.26, p > 0.05).
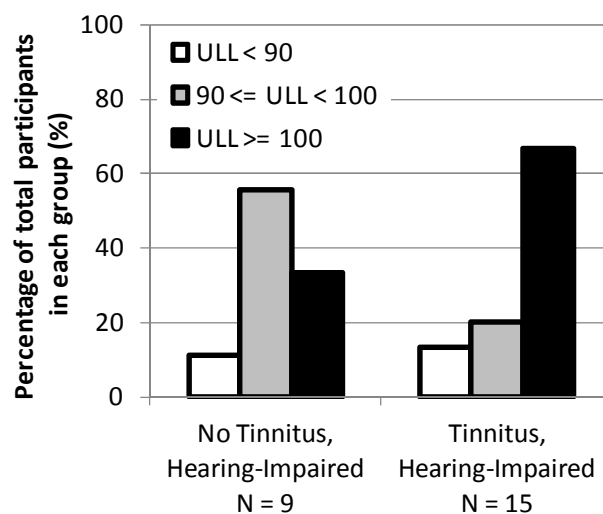
Figure 11.1: Average percentage of minimum Uncomfortable Loudness Levels for hearing-impaired listeners without tinnitus and hearing-impaired listeners with tinnitus, obtained below 90 dB SPL (white bar), between 90 and 100 dB SPL (grey bar) and above 100 dB SPL (black bar).

11.2 Percentage of Hearing-aid use between hearing-impaired groups

Some studies have suggested that hearing-aid users may acclimatise to higher tolerances of loud sounds after amplification (Byrne and Dirks, 1996; Munro and Trotter, 2006;

Olsen et al., 1999). The results of the previous analyses on uncomfortable loudness levels could therefore be affected by the different levels of acclimatisation, mediated by hearing-aid use in the two hearing-impaired groups. A Chi-Square Test for frequency tables was used to investigate if there was a similar number of hearing-aid versus non hearing-aid users within each of the two hearing-impaired groups. Although the graph in Figure 11.2 suggests a slightly higher proportion of tinnitus sufferers were not hearing-aid users, the differences were not statistically significant ($\chi^2(1) = 1.54$, $p > 0.05$).
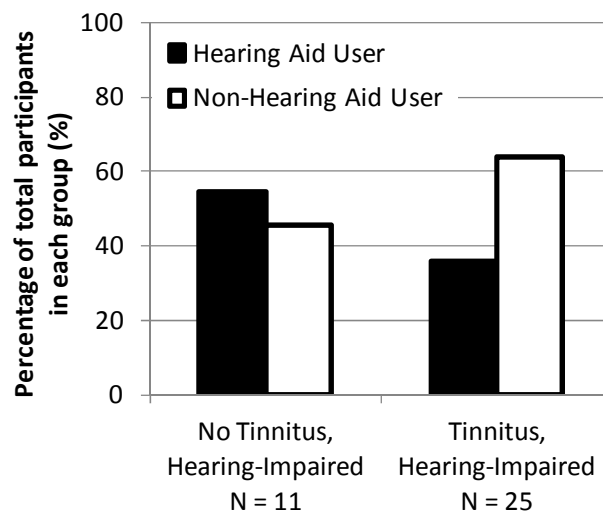
Figure 11.2: Distribution of hearing-aid users for hearing-impaired listeners with tinnitus and hearing-impaired listeners without tinnitus. Black bar represents proportion of hearing-aid user and white bar represent non-hearing-aid user.

11.3 Discussion

The ULLs were measured in this study as a means to understand how loud sounds are tolerated in the two hearing-impaired groups. The presence of recruitment or a rapid rise of intolerance to loud sounds may be caused by impairment to the outer hair cells, which are suggested to manage the compressive ability of the inner ear (Robles and Ruggero, 2001; Ruggero and Rich, 1991). No significant differences were found between the two hearing-

impaired groups. The usage of hearing-aids was also not found to be significantly different between the tinnitus and no tinnitus group, and it is not possible to deduce any differences in cochlear function between the two hearing-impaired groups with the two methods used.

A possible explanation for this result may be that ULLs alone may not be a sensitive enough measure of outer hair cell function. This is because the response produced by high levels signals can be influenced by a number of factors. The first is the acclimatisation of loud sounds with the use of hearing-aids. This is a commonly reported occurrence where hearing-aid users would gradually request for hearing-aids to be made louder after long periods of use (Olsen et al., 1999). Secondly, loudness tolerance may be modulated by the acoustic reflex, which has been shown to be able to adapt to very loud, or very quiet sound environments (Munro and Trotter, 2006; Munro and Blount, 2009). Finally, the use of high-level stimuli as a measure of recruitment would enforce the assumption that the loss of nonlinearity is present throughout the region that was stimulated. It is not known how the cochlea would tolerate high-level stimuli if only a *portion* of the area being stimulated had compressive capabilities.

11.4 Conclusions

The analyses in previous chapters provide evidence of better outer hair cell function in people with tinnitus, compared to those without tinnitus. Although the results in this chapter is in the expected direction (better tolerance for loud sounds and smaller proportion of hearing-aid users in the tinnitus group), the difference between the hearing-impaired groups were not significant. This could be caused by the small sample size investigated and that ULLS may be a crude measurement, which is influenced by a number of variables and insensitive to small changes in cochlear function.

Chapter 12
Distortion Product Otoacoustic Emissions

The presence of Distortion Product Otoacoustic Emissions (DPOAEs) is believed to be an objective indicator of functional outer hair cells, and is not affected by damage to the inner hair cells (Kemp, 2002; Wang et al., 1997). DPOAEs have been used as a tool to investigate the mechanisms of tinnitus, mostly in the normal-hearing populations (Acker, 2009; Granjeiro et al., 2008; Ozimek et al., 2006; Shiomi et al., 1997). These studies reported comparatively lower DPOAE amplitudes in people with tinnitus, thus suggesting outer hair cell impairment. On the contrary, Sztuka et al. (2010) and Gouveris et al. (2005) separately reported that the DPOAE amplitudes were much *higher* in groups of people with tinnitus, when compared to their normal controls. Sztuka et al. (2010) suggested that tinnitus may be triggered by increased motility of the outer hair cells (due to decreased efferent activity), and not by reduced outer hair cell function (due to missing hair cells, stereocilia fusion, and so on). These findings agree with Riga et al. (2007) who investigated the function of the efferent system in normal-hearing listeners with tinnitus and those without tinnitus. They recorded DPOAEs in the presence of contralateral white noise and reported that people with tinnitus appeared to have *less effective* functioning of the efferent system compared to their control group.

This chapter investigates DPOAE amplitudes between the hearing-impaired listeners with tinnitus and hearing-impaired listeners without tinnitus. Procedures to carry out DPOAE measurements were detailed in Section 3.3. DPOAE responses have not been measured and compared between these two groups in the past, presumably due to the higher probability of absent responses with increasing hearing impairment (Hall III, 2000). Hearing thresholds up to

50 dB loss has been suggested to be a result of outer hair cell loss (Hawkins et al., 1976), which

would partly explain the absence of DPOAEs when hearing thresholds are at about 50 dB SPL

because DPOAE responses are dependent on good outer hair cell function. However, absent

DPOAEs (dips and notches) are ambiguous because they can also be caused by variations of

acoustical properties of the ear, for instance, middle ear alterations in the elderly (Oeken et al.,

2000), and not necessarily by the absence of functional outer hair cells (Hall III, 2000).

Ipsilateral de-efferentation (olivocochlear bundle sectioning), in the presence of normal outer

hair cell count has also been observed to reduce DPOAE responses (Zheng et al., 1997b).

12.1   Average DPOAEs between groups
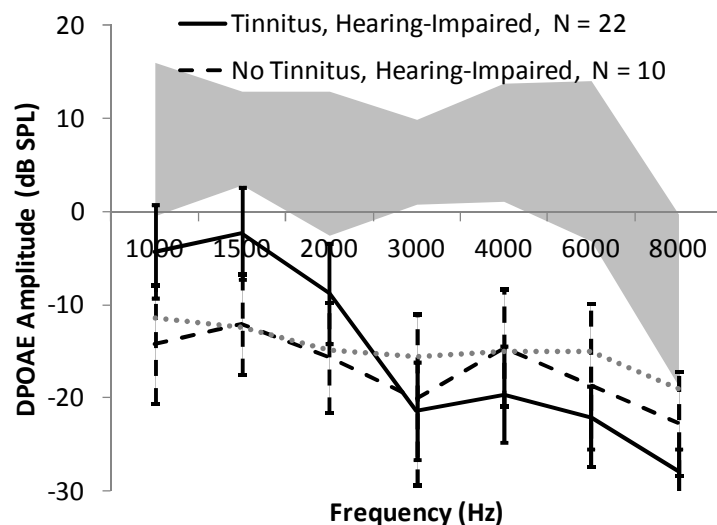
Figure 12.1: Average DPOAE amplitude responses (mean ± 95% C.I.) at different frequency for hearing-impaired listeners with tinnitus (solid line) and hearing-impaired listeners without tinnitus (dashed line). The grey dotted line represents the average noise floor. The grey area represents average DPOAE amplitude responses (mean ± 95% C.I.) for the normal-hearing group.

Figure 12.1 shows the average DPOAE responses at each frequency were compared

between hearing-impaired listeners with tinnitus and hearing-impaired listeners without

tinnitus. DPOAE responses in the tinnitus group present at 1000, 1500 and 2000 Hz, were above the noise floor. This suggests the presence of outer hair cell function at those frequencies in the tinnitus group. Unfortunately, none of the DPOAE responses in the no tinnitus group was above the noise floor, so it is not possible to deduce the presence of outer hair cell function in this group.

12.2 Discussion and conclusions

In this chapter, DPOAE measurements were compared between two hearing-impaired groups; one with tinnitus and the other without tinnitus. The comparison between the two groups showed strong DPOAE responses in hearing-impaired listeners with tinnitus between 1000 Hz and 2000 Hz. This was consistent with absolute threshold values in the same frequency range that was better in the tinnitus group compared to the hearing-impaired group without tinnitus. Unfortunately, the rest of the DPOAE responses, for both hearing-impaired groups, appeared below the noise floor, which means that it is not possible to dissociate these responses from random ambient noise. It is therefore not possible to explore differences that may be present between the two groups at these frequencies.

The presence of DPOAE responses are associated with good outer hair cell function (Kemp, 1986). However, the *absence* of DPOAE responses can be interpreted in a number of ways, and does not necessarily translate to impaired outer hair cell function (Hall III, 2000; Oeken et al., 2000; Zheng et al., 1997a). These include reduced outer hair cell function, acoustical variations and the damaged efferent pathways. Previous analyses in this thesis, on outer hair cell function (frequency selectivity and compression) suggest the possibility of functional but reduced outer hair cell performance in the tinnitus group. One explanation for this is that the psychophysical methods may be better at highlighting the reduction of outer

hair cell function than DPOAE measurements. Hofstetter et al. (1997) proposed a linear

relationship between DPOAE responses and outer hair cell damage. On average, a 3dB

reduction in DPOAE responses is associated with a 10% outer hair cell loss. This would mean

that about 30% outer hair cell damage would be enough to reduce DPOAE responses (by 10 dB

SPL) to below the noise floor, rendering them immeasurable.

Chapter 13
Discussions

This thesis aimed to understand why *only a proportion* of hearing-impaired individuals perceive tinnitus, despite the strong links between hearing impairment and tinnitus (Atherley et al., 1968; Loeb and Smith, 1967). In order to do so, behavioural measures of cochlear function were made and compared between hearing-impaired listeners with tinnitus and hearing-impaired listeners without tinnitus. The results of this thesis suggest the existence of two distinct types of hearing impairment, which can be predicted by the presence of tinnitus. Despite having similarly raised thresholds, tinnitus sufferers in this study had (1) steeper regions on their audiograms, (2) larger threshold differences between long and short tones, (3) less tendency to listen off-frequency, (4) better frequency selectivity and (5) showed a stronger presence of compression compared to those without tinnitus but with similarly raised thresholds. All of these observations suggest that people with tinnitus may have better outer hair cell function than those without tinnitus, despite having similarly raised thresholds.

The first analysis investigated whether or not there were differences in terms of absolute threshold measurements between the tinnitus and no tinnitus group. Chapter 5 compared the (1) average absolute thresholds, (2) pattern of thresholds across frequencies and (3) the area under the absolute thresholds between the two hearing-impaired groups. Only the third method used uncovered significant differences between the two hearing-impaired groups. This agreed with reports by König et al. (2006) who also observed a greater amount of impairment in people without tinnitus. König et al. (2006) used a greater number of measurement points compared to that carried out in this thesis. The choice of measurements

was aimed at mimicking standard clinical measurements. This suggested that König et al.'s (2006) method of calculating the area under the graph in order to estimate the amount of hearing loss present may be a more sensitive method of quantifying the amount of hearing loss that is suffered.

Chapter 6 investigated the predictions instigated by the 'Edge Effect' theory. Kiang et al. (1970) proposed that tinnitus may be caused by striking differences between normal and abnormal regions in the cochlea that may affect the pattern of spontaneous activity in the auditory nerve. They predicted that steep slopes in the audiogram are linked to regions where large differences between normal and impaired regions exist. Physiological observations by Eggermont and Roberts (2004) further proposed that the over-representation of the tonotopic map close to the 'edge' of normal-hearing, will give rise to tinnitus. The results of this chapter supported Kiang et al.'s (1970) proposal and the observations made by König et al. (2006). In other words, people with tinnitus had steeper slopes compared to those without tinnitus. However, the pitch of tinnitus was not at the 'edge' of normal-hearing, as suggested by the 'Edge Effect' theory. Instead, the perception of tinnitus was related to areas where hearing loss was present. This observation had been previously reported by a number of studies (Noreña et al., 2002; Roberts et al., 2008; Sereda et al., 2011). The presence of steeper slopes in people with tinnitus only suggests a great difference between normal and impaired regions in the inner ear. However, the exact configuration of cochlear damage that would result in steeper audiometric slopes, specifically in people with tinnitus, is unknown. Moore et al. (2000) suggested that sensorineural hearing-impairment is a function of both outer and inner hair cell damage. However, it is not possible to determine the exact balance of damage contributed by the individual systems. Additional measurements would be necessary for this purpose.

Outer and inner hair cell dysfunctions have both been suggested to trigger tinnitus. Kiang et al.'s (1970) hypothesis, for instance, would implicate the inner hair cells, because damage to the outer hair cells alone would have little or no impact on the auditory nerve's spontaneous activity (Dallos and Harris, 1978; Wang et al., 1997). However, the discordant theory (Jastreboff, 1990) suggests that imbalance between outer and inner hair cell responses to the central region would trigger the perception of tinnitus. This imbalance was proposed to be biased by outer hair cell defects, because outer hair cells were believed to be more vulnerable to damage (Hawkins, 1973; Hawkins et al., 1976). More recent physiological evidence, however, has refuted the claim that outer hair cells are the primary site of damage in hearing impairment. Kujawa and Liberman (2009) observed that normal-functioning outer hair cells could exist in the presence of damaged inner hair cells. These damaged inner hair cells would subsequently trigger inevitable neural degeneration. The idea of neural degeneration or deafferentation has been recently proposed as a trigger for tinnitus by a number of studies (Bauer et al., 2007; Weisz et al., 2006).

Chapters 8 to 12 compared behavioural measures of cochlear function between the two hearing-impaired groups, in light of new evidence that question the role of outer hair cells as a trigger for tinnitus. The tinnitus group was observed to have (1) larger threshold differences between long and short tones, (2) less tendency to listen off-frequency, (3) better frequency selectivity and (4) stronger presence of compression than hearing-impaired listeners without tinnitus. The combination of these observations suggest the possibility that people with tinnitus suffer from less outer hair cell impairment, which, according to Moore et al.'s (2000) equation, would implicate predominant inner hair cell damage instead. However, measures of uncomfortable loudness levels and distortion products otoacoustic emissions did not show significant differences between the two groups. This could have been attributed to problems

associated with the measurement of tolerance to loud sounds and the sensitivity of DPOAE measurements to mild outer hair cell dysfunction, which was discussed in Chapters 11 and 12.

The results of this thesis provide evidence in support of Bauer et al.'s (2007) study who reported minimal outer hair cell damage in their noise-traumatised animal models who also had tinnitus. The authors in Bauer et al.'s (2007) study used *moderately* loud noise stimuli to induce acoustic trauma, which would be a better approximation to the noise exposed to humans in everyday life (Saunders et al., 1985; Schmiedt, 1984). Bauer et al. (2007) observed minimal hair cell damage in their noise traumatised rat models, which were behaviourally trained to indicate the presence of tinnitus. They reported that the amount of tinnitus was correlated with low auditory fibre density in the cochlea. The authors also observed selective loss of large diameter fibres (characterised by high spontaneous firing rates and low thresholds). High spontaneous rate (HSR) fibres make up most of the somatic connections to cells in the dorsal cochlear nucleus (DCN), where neural correlates of tinnitus have been reported (Kaltenbach et al., 1992; Liberman, 1993). Bauer et al. (2007) suggested that the loss of HSR connections to the DCN (a source of inhibition to the fusiform cells may trigger an elevation of the spontaneous rates in the fusiform cells, which causes the brain to perceive a phantom sound. Unfortunately, there is no known psychoacoustic measure to specifically test for the performance of these high spontaneous rate fibres.

The results of this thesis provide psychophysical evidence in support of Bauer et al.'s (2007) observations. These psychophysical results reported in this thesis have not been reported by any previous studies. The present data suggest the possibility that the tinnitus group may suffer from predominantly inner hair cell damage, which leads on to gradual neural degeneration. Conversely, those without tinnitus may have comparatively greater outer hair cell damage. Outer hair cell damage without any loss of tonic activity to the dorsal cochlea

nucleus (as opposed to reduced acoustically-driven input from the periphery) may explain why

some people with hearing impairment do not perceive any phantom sounds. Reduction of

spontaneous activity may also cause reduced tonic activation of cells in central auditory

structures and may be the main trigger of tinnitus. This could be due to damage to the inner

hair cells (random transmitter release), or the spiral ganglion cells, both of which are suggested

sources of spontaneous activity in the cochlea (Manley and Robertson, 1976). A schematic of

the relationship between hair cell and afferent neurons is shown in Figure 13.1.
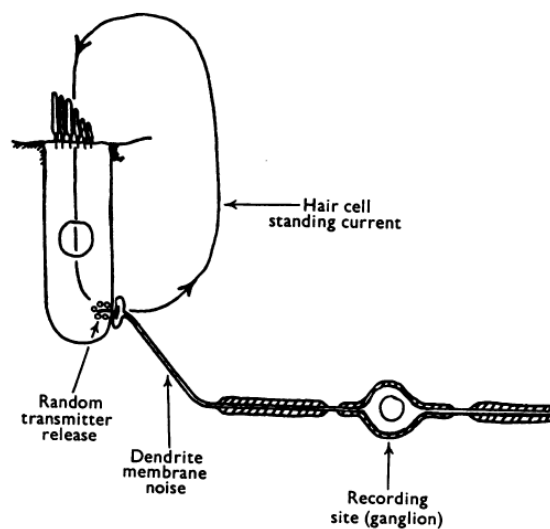
Figure 13.1: Schematic of the relationship between hair cell and afferent neuron, adapted from Manley and Robertson (1976).

There is growing evidence that implicates structures from the inner hair cells and

beyond, as the main triggers of tinnitus. Tinnitus-inducing pharmacological drugs like

salicylates, for instance, were once speculated to have a greater impact on outer hair cell

function. However, more recent evidence have shown that spiral ganglion cells and neural

degeneration also occur together with outer hair cell damage (Peng et al., 2003). Quinine,

another known tinnitus-inducing drug, selectively reduces the number of high spontaneous rate

fibres without any detrimental effects to the neural tuning curves (and inferred outer hair cell function) (Mulheran, 1999). Furosemide, which also induces tinnitus, decreases the endocochlear potential. This has a direct impact on the receptor potential of inner hair cells, and a temporary effect on the outer hair cells (Sewell, 1984b). Carboplatin, a chemotherapy drug that induces tinnitus as a side-effect, selectively disrupts inner hair cell function (fusion, extrusion and loss of stereocilia), while sparing a large proportion of outer hair cells (Wake et al., 1994; Wang et al., 1997). Lastly, cisplatin, also a tinnitus-inducing drug, reduces outer hair cell function and promotes neural degeneration (Kopke et al., 1999). Inner hair cell damage and/or neural degeneration (either by damage to the hair cells, or to the spiral ganglion cells) are both common factors in *all* the above-mentioned tinnitus-inducing drugs.

Presbycusis may also be related to decrease spontaneous activity. The effects of the aging process on the endocochlear potential have been often simulated with the use of furosemide, which causes endocochlear potential reduction. The loss of low spontaneous rate fibres were reportedly more prevalent when endocochlear potential was reduced, compared to the high spontaneous rate fibres (Lang et al., 2010; Sewell, 1984a). This is in contrast with Bauer et al.'s (2007) observations of the predominant loss of high spontaneous rate fibres in their tinnitus models. However, it is possible that the loss of spontaneous activity from any source, as long as it exceeds some critical value, is able to trigger the perception of tinnitus.

The loss of tonic activation to central cell structures may also be able to explain the occurrences of other forms of tinnitus. Otosclerosis, for instance, is another medical condition that may give rise to tinnitus (Nuttall et al., 2004). Recently, Doherty and Linthicum (2004) reported that cochlear calcification, due to otosclerosis may affect the stria vascularis, thus reducing the endocochlear potential, and disrupting the biochemical balance in the cochlea. In the case of Ménière's Disease, another tinnitus-associated condition, excess fluid develops in

the inner ear, together with degeneration of the spiral ganglion cells (Nadol et al., 1995). Other tinnitus-related otologic conditions are also related to neural dysfunctions. These include vestibular schwannomas, temporal mandibular joint disorders, multiple sclerosis and facial palsy. However, there also exist other tinnitus-related otologic conditions where neural dysfunction may not be involved, or instance, external ear canal occlusion (impacted wax), otitis media and tympanic membrane perforation. In fact, it is often reported clinically, by tinnitus sufferers, that the perception of their tinnitus seem to worsen when they have a cold. It is possible that this may be a consequence of reduced sound input from the environment, which is analogous to normal-hearing individuals who *only* perceive phantom noises in very quiet environments (Heller and Bergman, 1953). This may be a form of adaptation to the new acoustic environment, in the same way that the pupils in the eye adjust to a darkened room.

The analyses that were made in this thesis were based on the assumption that other factors, such as recovery from forward-masking, are equally present, or equally damaged in both hearing-impaired groups. However, if impairment to the inner hair cells affects the rate of neurotransmitter refill or depletion at the synaptic cleft, then the recovery from forward-masking may be affected (Meddis and O'Mard, 2005). This would result in shallower Temporal Masking Curves, even if compression is not impaired. Shallow TMCs can also manifest if the level of the masker remains below compression threshold (30 to 40 dB SPL). This would explain the presence of abnormally shallow TMCs in some normal-hearing listeners, but not in the hearing-impaired group, because they were tested at probe levels that are within the compression thresholds (about 40 to 80 dB SPL).

The Threshold Equalising Noise (TEN) test was developed as a method to infer inner hair cell function (Moore et al., 2000). However, it was not used in this study because of the complications associated with the measurements. The TEN test makes use of a spectrally-

shaped noise that produces the same amount of masking across all frequencies when measured in people with normal-hearing. A dead region (areas with suspected inner hair cell dysfunction) is inferred to be present when the masked threshold is at least 10 dB above the absolute threshold *and* 10 dB above the level of the TEN noise. The TEN test was not used in this study because it requires participants to be tested at high signal levels that often exceed 90 dB SPL. People with tinnitus usually have hearing losses at high frequencies and in some cases, presence of hyperacusis (Gold, 2003). Some participants also reported that loud noises sometimes exacerbate their tinnitus, so testing them at high signal levels may cause discomfort so it was not carried out. The only known study that investigated the use of the TEN test in people with tinnitus was conducted by Weisz et al. (2006). They tested normal-hearing listeners with tinnitus, and reported that suspected inner hair cell damage was present in the group. This agrees with the results presented in this thesis. Unfortunately, the small number of normal-hearing participants with permanent tinnitus, in this study, made it difficult to analyse cochlear function in this group.

Clinical relevance of findings

The findings of this thesis are consistent with the possibility that the lack of tonic activity to central cell structures, because of reduced spontaneous activity in the auditory nerve, are responsible for triggering plastic processes that lead to the perception of phantom sound. The maintenance of tonic activity may be able to prevent the onset of tinnitus. This possibility was explored by Noreña and Eggermont (2006). In their study, they investigated the effect of an enriched acoustic environment on cats after noise trauma. Cats that were placed in the acoustically enriched environment did not exhibit any of the neural correlates of tinnitus (hyperactivity in the dorsal cochlea nucleus). On the contrary, cats that were placed in a quiet

environment, post trauma, demonstrated hyperactivity in the dorsal cochlea nucleus, which has been cited to be a neural correlate of tinnitus (Kaltenbach et al., 1998). This could be a result of neural compensation to maintain tonic activation to central cell structures. Kujawa and Liberman (2009) explains that this is possible if the discharge rate in the remaining neurons is increased, or if the number of neurons that respond to stimuli are increased. Clinically, the findings are in favour of rapid aural rehabilitation, even in very mild hearing losses. The onset of tinnitus can be viewed as a manifestation of weakening activity to the central structures, which may be reversed if timely rehabilitation is provided.

This study also showed the existence of two distinct classes of sensorineural hearing impairment. A number of earlier studies had explored this possibility. Histopathological studies by Schuknecht (1993) suggested four classifications of presbycusis, which were sensory, neural, strial and cochlear conductive dysfunctions. Psychoacoustical studies differentiated between cochlear and retrocochlear pathologies (Brunt, 2002; Olsen, 1987). However, these psychoacoustical tests were often relegated to the research field or used predominantly to identify vestibular schwannomas. The diagnosis between cochlear and retrocochlear pathologies is sometimes performed clinically, but the merit of this diagnosis has little impact on the treatment of the individual, such as hearing-aid prescription. This study suggests two distinct classes of hearing impairment. People with tinnitus may have mostly inner hair cell dysfunction, while those without tinnitus may have outer hair cell dysfunction. The assumption that *all* hearing-impaired people have loss of compression and poor frequency selectivity is *not* met. This suggests the possibility for two separate types of rehabilitation for the two groups of hearing impairment. If the tinnitus group has mostly inner hair cell dysfunction, then a simple gain-recovery strategy might be all that is required. The no tinnitus group, on the other hand, may require more complex signal-processing strategies to compensate for the loss of

compression and reduced frequency selectivity. As a result, the presence (or absence) of tinnitus may be a simple marker to classify hearing-impairment and to improve on the way hearing-aids are prescribed.

To summarise, the study in this thesis set out to understand the type of cochlear damage that triggers the perception of tinnitus in hearing-impaired listeners. Behavioural measures of cochlear function were made and it was found that this differed between hearing-impaired listeners with tinnitus and those without tinnitus but who were also hearing-impaired. The pattern of hearing loss in the group with tinnitus is suggestive of a cochlear pathology that is consistent with inner hair cell or neural damage (Kujawa and Liberman, 2009; Liberman and Dodds, 1984). Hearing-impaired listeners without tinnitus, however, displayed hearing loss patterns that were consistent with outer hair cell dysfunction.

The novelty of the findings in this thesis was possible due to the set of detailed hearing measurements that are currently not standard practice in clinics. The differences in cochlear function between the two hearing-impaired groups suggest the need for individualised modes of rehabilitation. Unfortunately, time constraints that are placed in clinics mean that it may not always be possible to make very detailed measurements. The ability to quickly identify a specific pattern of hearing loss, using the presence of tinnitus, may thus, provide a quick solution to the type of aural rehabilitation required without the need for extensive hearing tests.

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Zenner, H.P., Ernst, A. 1993. Cochlear-motor, transduction and signal-transfer tinnitus: models for three types of cochlear tinnitus. Eur Arch Otorhinolaryngol 249, 447-54.

Zheng, X.Y., Henderson, D., McFadden, S.L., Hu, B.H. 1997a. The role of the cochlear efferent system in acquired resistance to noise-induced hearing loss. Hear Res 104, 191-203.

Zheng, X.Y., Henderson, D., Hu, B.H., Ding, D.L., McFadden, S.L. 1997b. The influence of the cochlear efferent system on chronic acoustic trauma. Hear Res 107, 147-59.

Appendices

A) Letter of invitation to participants

11 April 2011

Letter of invitation

Dear Sir/ Madam,

Re: Volunteering for Tinnitus and Hearing Deficits Research

The Hearing Research Laboratory at the University of Essex will be working together with Mr. Don McFerran, ENT Consultant at Essex County Hospital on a study about tinnitus. In order to achieve this, we hope to recruit participants with tinnitus and / or normal hearing and a control group without tinnitus.

Enclosed with this letter is an information pack about the study. Part 1 of the Participant Information Sheet provides the important basic details about the study. Part 2 lists more detailed information which should answer any additional questions that you may have. Please take your time to read through the information and do contact any one of the researchers if you have any further questions about the study.

If you have happy to participate in the study, please complete and sign the **consent form** and post it back to us in the pre-paid envelope provided. If you do not wish to participate, kindly complete the section below and post it back to us in the envelope provided. Once we have received the consent forms, the Chief Investigator, Miss Christine Tan will contact you for your first appointment at the University of Essex.

Thank you for your time.

Best regards,

Christine Tan
Chief Investigator
PhD Student
Hearing Research Laboratory
University of Essex

Kindly tear or cut along the dotted lines and post it back in the pre-paid envelope provided.

- I do not wish to participate in the research. ☐

Signed: .... **Date:** ....

Name: ....

B) Participant Information Sheets

Participant Information Sheet – Part 1/2

Project title: Tinnitus and Hearing Deficits

We would like to invite you to take part in a research study. Before you decide, you will need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully.

(Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study).

Included at the end of this information sheet are contact details of the researchers involved in this study. You are encouraged to contact them should you need more information about this study. Take time to decide whether or not you wish to take part.

Introduction
This study is done as part of a three year doctoral degree programme. The aim of this study is to identify the relationship between specific hearing patterns and tinnitus. A series of routine hearing tests will be performed as well as more detailed hearing tests. This will provide a comparison between the different test strategies and help identify the best means of detecting defects in the cochlear.

Why have I been invited?
The Hearing Research Laboratory at the University of Essex will be working together with Mr. Don McFerran, ENT Consultant at Essex County Hospital on a study about tinnitus. In order to achieve this, we hope to recruit participants with tinnitus and/ or normal hearing, and a control group without tinnitus.

Do I have to take part?
It is up to you to decide. Take your time to read this information sheet which will provide you with important information about this study. If you are unsure about the project and would like to ask someone, please contact any one of the researchers named in this study. When you are ready and have agreed to take part, please sign the consent form and post it back to us in the envelope provided.

Can I leave at anytime?
Yes. If you decide to take part and then later change your mind, either before you start the study or during it, you can withdraw without giving your reasons. If you wish, your data will be destroyed. Whether or not you chose to participate in this study will not affect the quality of NHS service that you are receiving or will receive in the future.

What will happen to me if I take part?
Once you have signed and posted back the consent form, you will be contacted by the Chief Investigator, Christine Tan, to arrange for sessions at the University of Essex. The whole study will take approximately 10 hours, but this a rough estimation as the duration will depend on the complexity of your hearing condition and your ability to perform in the tasks. The recommended duration for each session is 2 hours, with breaks every half hour or as

needed. However, the duration of each session will be highly flexible and tailored to suite your schedule.

If you have tinnitus, you will be asked to complete two questionnaires and a structured interview. The questionnaires are about your tinnitus and how well you cope with it. The scores on these two questionnaires will determine if you are eligible to participate in the rest of the study. This is done because the research is aimed at investigating stable forms of tinnitus. You will then be asked to complete a short structured interview. You do not have to answer all the questions in the interview, but they might be able to provide us with more information about other conditions that may affect your tinnitus.

The tasks performed at the university involve more detailed hearing tests. In these tests, you will be required to wear headphones (without hearing aids) and be seated in a sound-proofed room. The task will require you to count the number of tones that you are able to hear, by pressing the appropriate buttons. The next set of tasks will involve identifying the frequency of the tinnitus and the minimum amount of noise that is able to make the tinnitus seem quieter.

The last set of measurements will involve the use of equipment already used in the NHS service for hearing screening in newborn infants. These are non-invasive measurements. All the measurements will require you to be very relaxed (or asleep) while sounds are being played to you through soft foam ear tips that are placed at the entrance of your ears. Recording leads will be placed on your head and behind your ears to measure responses from your inner ear. The recording leads will be attached to your skin with a hypoallergenic gel that is easily washed away with warm water.

Will my data be anonymous?
Yes. All information collected about you will be kept anonymous.

Are there any risks to my hearing?
No. All possible precautions have been made to ensure that the sounds used in this study will not be painful to hear.

What are the possible benefits of taking part?
We cannot promise the study will help you but the information we get from this study will help improve the treatment and understanding of tinnitus. You are also reminded that the study is researched based, and the University researchers are not able to supply a medical diagnosis or offer advice regarding treatment. If you have any questions in this respect, you should contact your consultant at Essex County Hospital, or your General Practitioner.

Should you require additional information or need to ask any further questions before deciding whether or not to participate in this study, kindly direct all correspondence to one of the following researchers:

Christine Tan, MSc. Audiology   Mr. Don McFerran, FRCS ORL-HNS
PhD Student   ENT Consultant
Room 2.729, Dept of Psychology   ENT Department
University of Essex   Essex County Hospital
Wivenhoe Park   Lexden Road
Colchester CO4 3SQ   Colchester CO3 3NB
Tel: 01206 873941   Tel: 01206 744493
Email: ctan@essex.ac.uk   Email: donald.mcferran@colchesterhospital.nhs.uk

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

Participant Information Sheet – Part 2/2

Project title: Tinnitus and Hearing Deficits

This section provides further information about the above study.

Expenses and payment
You will not be paid for your participation, but all your travel expenses and parking fees to and from the University of Essex during the course of the study will be reimbursed. If you are a First-year Psychology student, you will be given the adequate amount of credits for the module that you are taking. You will also be given the chance to win one of five £10 Waterstone's vouchers.

Involvement of the General Practitioner / Family Doctor (GP)
Your GP will be informed about the study and your participation in the study. Any conditions uncovered during the course of the study that may require medical attention will be made known to your GP.

Will my taking part in this study be kept confidential?
If you join this study, some parts of your medical records and the data collected for the study will be looked at by authorised persons from the research team. They may also be looked at by representative of regulatory authorities and by authorised people to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty.

What will happen to the results of the research study?
The data that will be collected from you will be made anonymous by means of a participant identification code. The results from the study may be presented in scientific publications or at conferences.

Who is organising and funding the research?
The 3 year doctoral project is funded by the Royal National Institute for Deaf People (RNID).

Who has reviewed the study?
All research in the NHS is looked at by independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given favourable opinion by the Essex1 Research Ethics Committee.

What if there is a problem?
If you have a concern or are unhappy about any aspect of this study, you should contact the named researchers in Part 1 of the Participant Information Sheet. Otherwise, please contact:

Professor Ray Meddis, Director of Hearing Research Laboratory
Department of Psychology, University of Essex
Wivenhoe Park
Colchester CO4 3SQ
Tel: 01206 874882
Email: rmeddis@essex.ac.uk

C) Consent Forms

PIC:

Consent Form

Project title: Tinnitus and Hearing Deficits

Please tick

1. I confirm that I have read and understood Part 1 and Part 2 of the participant information sheet dated 02/12/2008 (version 1.2) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, and without my medical or legal rights being affected.

☐

3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by the investigating researchers, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

☐

4. I agree to have my data used anonymously for scientific purposes (publication in scientific journals, to be presented at conferences and so on).

☐

5. I understand that my GP will be notified of my participation in this study and of any outcome of this study that may require medical attention.

☐

6. I agree to take part in the above study.

☐

_____   _____   _____
Name of Participant   Date   Signature

_____   _____   _____
Name of Researcher   Date   Signature

Note: Kindly return this Consent Form in the envelope provided. A copy of this form will be posted out to you as soon as possible. Thank you.

Consent_Form version 1.2 (02/12/2008)   1/1

D) Tinnitus Handicap Inventory

University of Essex

PIC:

THI Questionnaire
Project title: Tinnitus and Hearing Deficits

Instructions: The following questions are designed to find out how much your tinnitus is affecting your day to day life. The questions can be answered "yes", "sometimes" or "no". It is important to answer all the questions, even if they do not seem to apply to you.

	Yes	Sometimes	No
1. Because of your tinnitus is it difficult for you to concentrate?	☐	☐	☐
2. Does the loudness of your tinnitus make it difficult for you to hear people?	☐	☐	☐
3. Does your tinnitus make you angry?	☐	☐	☐
4. Does your tinnitus make you confused?	☐	☐	☐
5. Because of your tinnitus do you feel desperate?	☐	☐	☐
6. Do you complain a great deal about your tinnitus?	☐	☐	☐
7. Because of your tinnitus do you have trouble falling asleep at night?	☐	☐	☐
8. Do you feel as though you cannot escape your tinnitus?	☐	☐	☐
9. Does your tinnitus interfere with your ability to enjoy social activities (such as going out to dinner or to the cinema)?	☐	☐	☐
10. Because of your tinnitus do you feel frustrated?	☐	☐	☐

11. Because of your tinnitus do you feel that you have a terrible disease? ☐ ☐ ☐

12. Does your tinnitus make it difficult for you to enjoy life? ☐ ☐ ☐

13. Does your tinnitus interfere with your job or household responsibilities? ☐ ☐ ☐

14. Because of your tinnitus do you find that you are often irritable? ☐ ☐ ☐

15. Because of your tinnitus is it difficult for you to read? ☐ ☐ ☐

16. Does your tinnitus make you upset? ☐ ☐ ☐

17. Do you feel that your tinnitus problem has placed stress on your relationship with members of your family and friends? ☐ ☐ ☐

18. Do you find it difficult to focus your attention away from your tinnitus and onto other things? ☐ ☐ ☐

19. Do you feel that you have no control over your tinnitus? ☐ ☐ ☐

20. Because of your tinnitus do you often feel tired? ☐ ☐ ☐

21. Because of your tinnitus do you often feel depressed? ☐ ☐ ☐

22. Does your tinnitus make you feel anxious? ☐ ☐ ☐

23. Do you feel that you can no longer cope with your tinnitus? ☐ ☐ ☐

24. Does your tinnitus get worse when you are under stress? ☐ ☐ ☐

25. Does your tinnitus make you feel insecure? ☐ ☐ ☐

University of Essex

THI Scores (Newman et al., 1996; McCombe et al., 2001)

Score	"Yes"	4
	"Sometimes"	2
	"No"	0

Total score	Interpretation	Grade
0-16	Slight (Only heard in quiet environments)	Grade 1
18-36	Mild (Easily masked by environmental sounds and easily forgotten with activities)	Grade 2
38-56	Moderate (Noticed in presence of background noise, although daily activities can still be performed)	Grade 3
58-76	Severe (Almost always heard, leads to disturbed sleep patterns and can interfere with daily activities)	Grade 4
78-100	Catastrophic (Always heard, disturbed sleep patterns, difficulty with any activities)	Grade 5

References:
McCombe A., Baguley D., Coles R., McKenna L, McKinney C., et al. 2001. Guidelines for the grading of tinnitus severity: the results of a working group commissioned by the British Association of Otolaryngologists, Head and Neck Surgeons, 1999. *Clin Otolaryngol Allied Sci*, 26, 388-393.
Newman C.W., Jacobson G.P. & Spitzer J.B. 1996. Development of the Tinnitus Handicap Inventory. *Arch Otolaryngol Head Neck Surg*, 122, 143-148.

E) Structured Interview

PIC:

Structured Interview
Project title: Tinnitus and Hearing Deficits

1. Do you remember when you first noticed your tinnitus?

_____

_____

2. Can you describe your tinnitus?

_____

_____

	Yes	Sometimes	No
3. Do you work in a noisy environment?	☐	☐	☐
4. Is it hard for you to open your mouth?	☐	☐	☐
5. Is it hard for you to move your jaw from side to side?	☐	☐	☐
6. Do you get tired or feel any pain while chewing?	☐	☐	☐
7. Do you have frequent headaches?	☐	☐	☐
8. Do you have pain or stiff neck?	☐	☐	☐
9. Do you have constant earaches?	☐	☐	☐
10. Do you hear clicking sounds when you chew or open your mouth?	☐	☐	☐
11. Do you clench or grind your teeth?	☐	☐	☐
12. Do you feel that your teeth are not aligned well?	☐	☐	☐

F) Tinnitus Modulation Manoeuvre Checklist

Tinnitus Modulation Maneuver Checklist

		Significantly Better		Mildy Better		No Change		Mildly Worse		Significantly Worse	
CN III, IV, & VI	Left Gaze	1	2	3	4	5	6	7	8	9	10
	Right Gaze	1	2	3	4	5	6	7	8	9	10
	Up Gaze	1	2	3	4	5	6	7	8	9	10
	Down Gaze	1	2	3	4	5	6	7	8	9	10
	Up-right Gaze	1	2	3	4	5	6	7	8	9	10
	Up-left Gaze	1	2	3	4	5	6	7	8	9	10
	Down-right Gaze	1	2	3	4	5	6	7	8	9	10
	Down-left Gaze	1	2	3	4	5	6	7	8	9	10
CN V	Jaw Clench Bilateral	1	2	3	4	5	6	7	8	9	10
	Jaw Clench Left	1	2	3	4	5	6	7	8	9	10
	Jaw Clench Right	1	2	3	4	5	6	7	8	9	10
CN VII	Eyebrow Raise	1	2	3	4	5	6	7	8	9	10
	Tight Eyelid Closure	1	2	3	4	5	6	7	8	9	10
	Wide Smile	1	2	3	4	5	6	7	8	9	10
	Lip Purse	1	2	3	4	5	6	7	8	9	10
	Cheek Blow	1	2	3	4	5	6	7	8	9	10
CN XI	Neck Flexion (Passive)	1	2	3	4	5	6	7	8	9	10
	Neck Flexion (Active)	1	2	3	4	5	6	7	8	9	10
	Neck Flexion (Active w/ Resistance)	1	2	3	4	5	6	7	8	9	10
	Neck Extension (Passive)	1	2	3	4	5	6	7	8	9	10
	Neck Extension (Active)	1	2	3	4	5	6	7	8	9	10
	Neck Extension (Active w/ Resistance)	1	2	3	4	5	6	7	8	9	10
	Left Lat. Flexion (Passive)	1	2	3	4	5	6	7	8	9	10
	Left Lat. Flexion (Active)	1	2	3	4	5	6	7	8	9	10
	Left Lat. Flexion (Active w/ Resistance)	1	2	3	4	5	6	7	8	9	10
	Right Lat. Flexion (Passive)	1	2	3	4	5	6	7	8	9	10
	Right Lat. Flexion (Active)	1	2	3	4	5	6	7	8	9	10
	Right Lat. Flexion (Active w/Resistance)	1	2	3	4	5	6	7	8	9	10
	Left Rotation (Passive)	1	2	3	4	5	6	7	8	9	10
	Left Rotation (Active)	1	2	3	4	5	6	7	8	9	10
	Left Rotation (Active w/ Resistance)	1	2	3	4	5	6	7	8	9	10
	Right Rotation (Passive)	1	2	3	4	5	6	7	8	9	10
	Right Rotation (Active)	1	2	3	4	5	6	7	8	9	10
	Right Rotation (Active w/Resistance)	1	2	3	4	5	6	7	8	9	10
	Shoulder Shrug (Active)	1	2	3	4	5	6	7	8	9	10
	Shoulder Shrug (Active w/Resistance)	1	2	3	4	5	6	7	8	9	10
CN XII	Tongue Protrusion (Midline)	1	2	3	4	5	6	7	8	9	10
	Tongue Protrusion (Left)	1	2	3	4	5	6	7	8	9	10
	Tongue Protrusion (Right)	1	2	3	4	5	6	7	8	9	10

G) Summary of Hearing Profiles

Some of the hearing profiles that will be analysed in subsequent chapters are summarised in this chapter. This allows for a general overview on the different types of hearing-impairment encountered in this study. The hearing profiles were allocated individual codes, and arranged in alphabetical order in this chapter. Readers will be able to make quick searches for individual hearing profiles if they are referenced in later chapters. The hearing profiles were categorised in three groups; (1) Normal-hearing, (2) No tinnitus and hearing-impaired and (3) Tinnitus and hearing-impaired. The hearing profiles were also separated according to unilateral or bilateral measurements. In some cases, bilateral measurements were possible where participants were willing to provide consent for extra testing time.

Missing data was unavoidable due to partial participation, drop-outs due to unforeseen circumstances, or because the probe thresholds were too high to be measured. Measurements were sometimes performed at odd frequencies to investigate the pattern of behaviour across frequencies. The top panel of the Hearing Profiles displays the TMC graphs (measure of compression, see Chapter 10). These TMC measurements were made at the corresponding IFMC frequency. Blank TMC graphs were sometimes unobtainable due to the reasons mentioned previously.

In some participants, additional absolute threshold and IFMC measurements were made either to investigate the emerging trend across frequency or to examine abnormal trends at an adjacent frequency. DPOAE responses were obtainable in some participants. The criteria for defining the presence of DPOAEs were explained earlier in Section 3.3. The noise floor and DPOAE responses were both shown in the Hearing Profiles.

Figure 0.1: Summary of hearing profiles of the three groups (normal-hearing, no tinnitus and hearing-impaired, and tinnitus and hearing-impaired). The top panel of a hearing profile represents the Temporal Masking Curve measures at various frequencies (filled triangles). The middle panel shows absolute thresholds measured using long durations (solid line, left axis) and short durations (dashed line, left axis), frequency selectivity (solid line, with probe frequency indicated by an open circle, left axis) and uncomfortable loudness level (open triangle, left axis). The Tinnitus Spectrum is represented by filled diamonds (right axis). The bottom panel shows the DPOAE responses (square) where present and the associated amount of noise (dotted line).

Normal-hearing
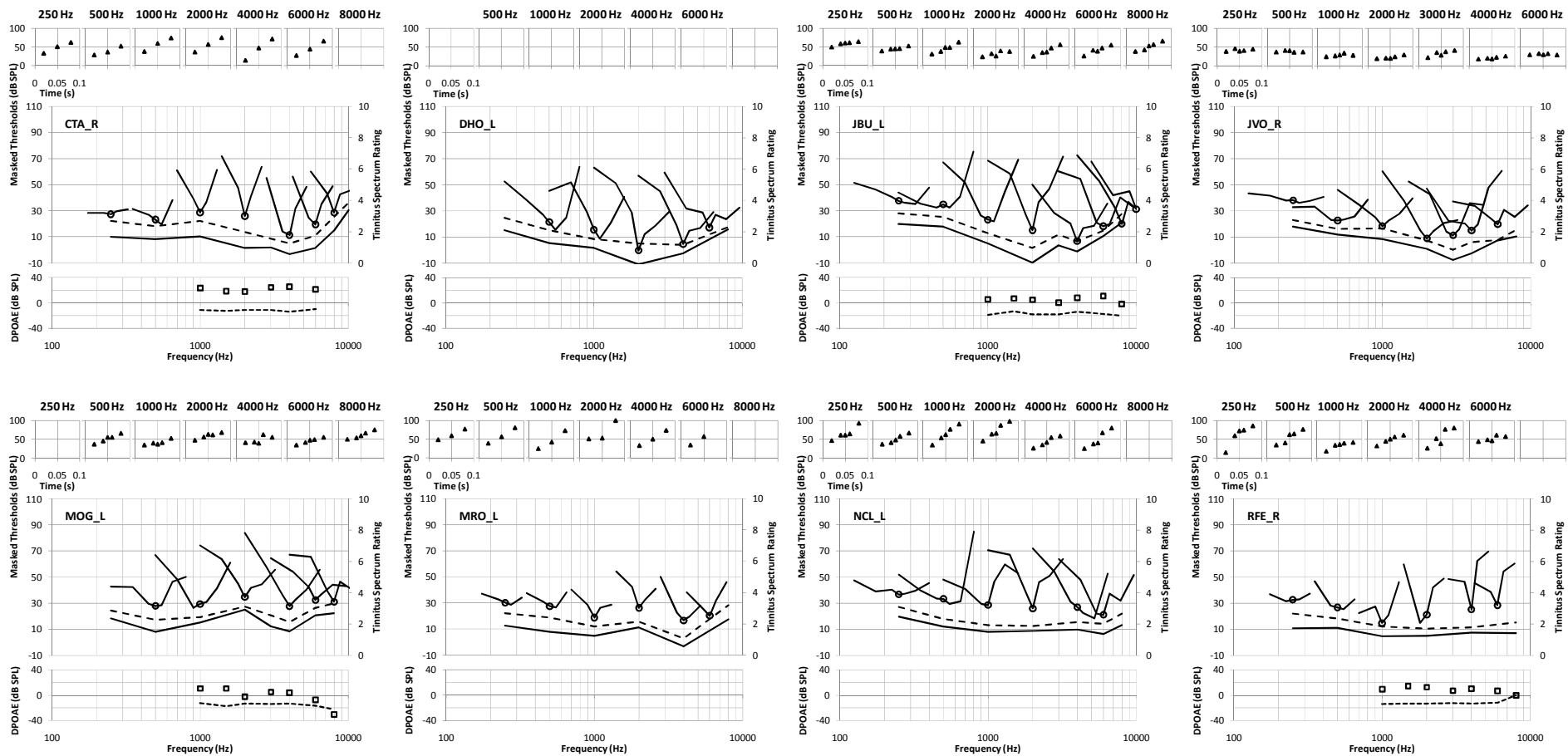
Normal-hearing
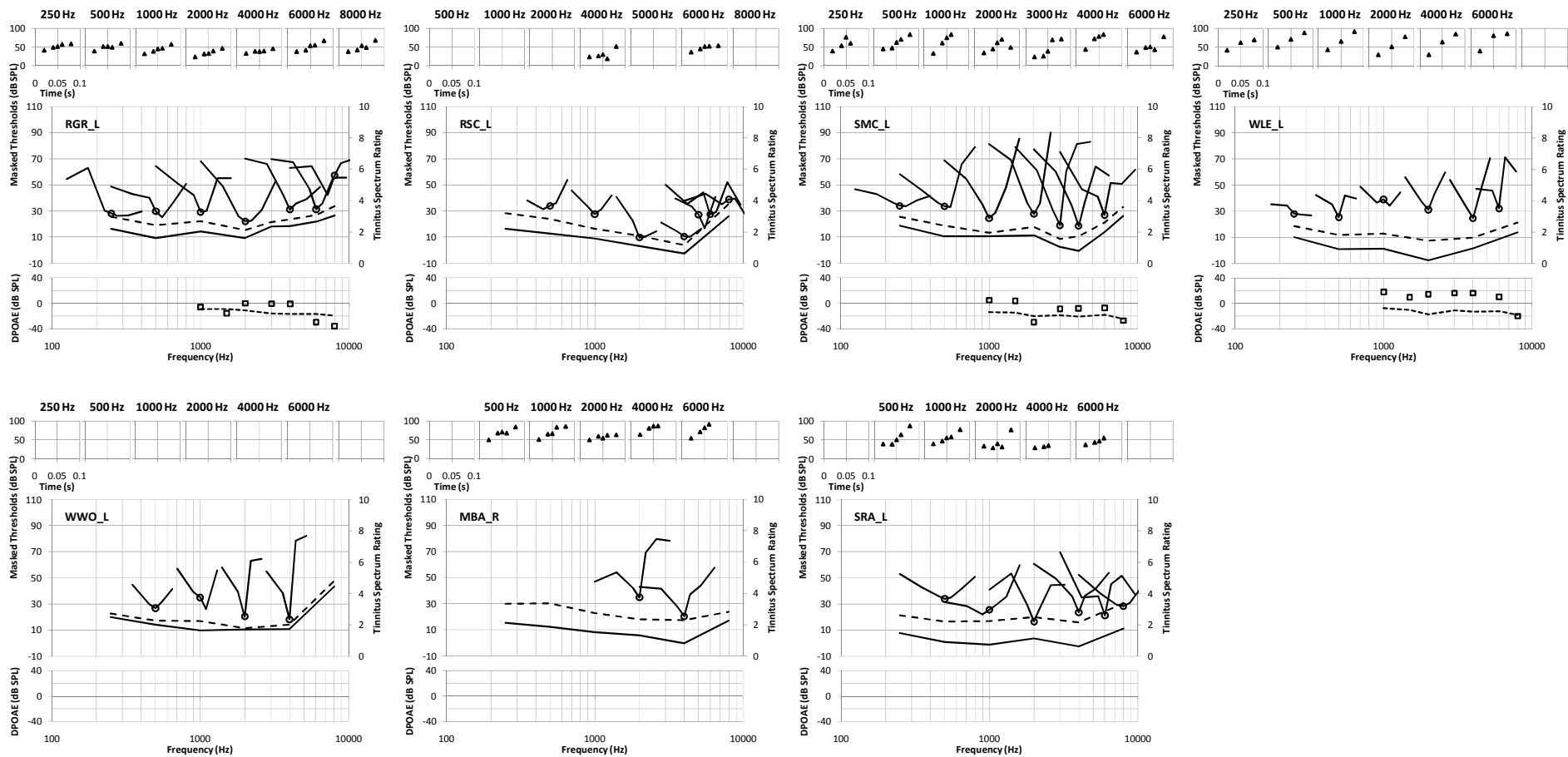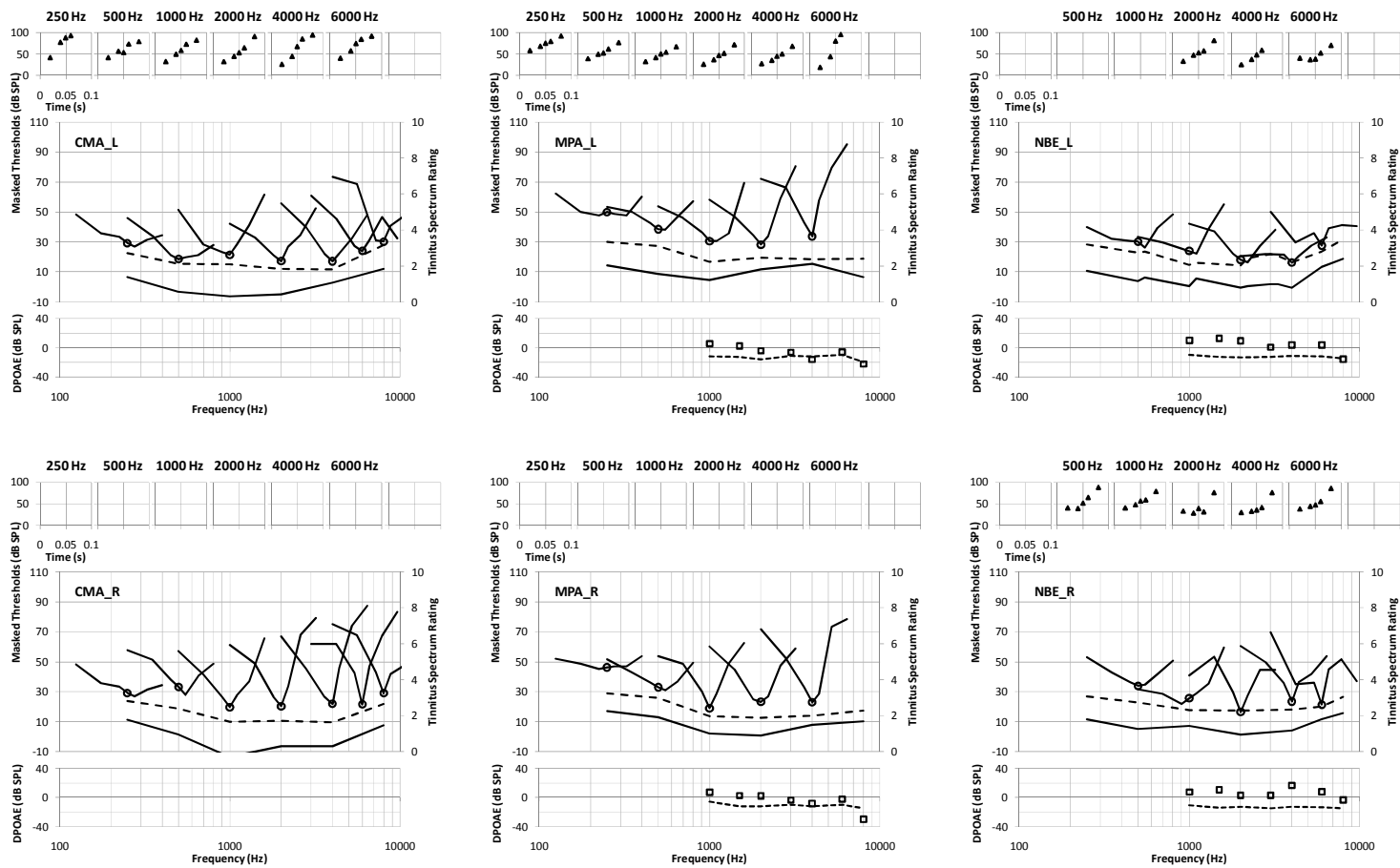
Normal-hearing

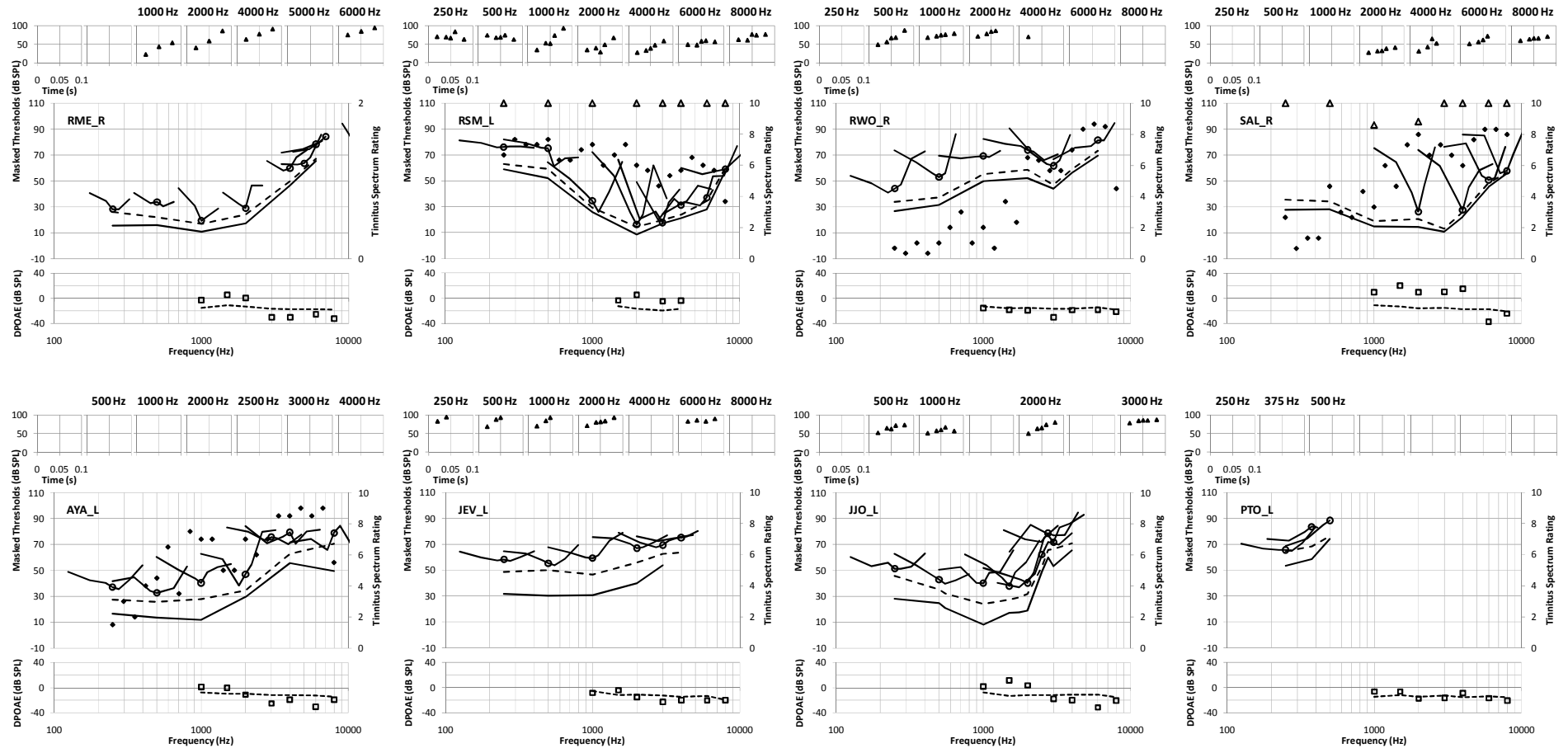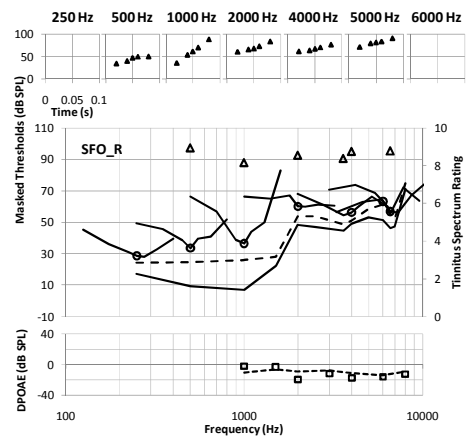# No Tinnitus, Hearing-Impaired
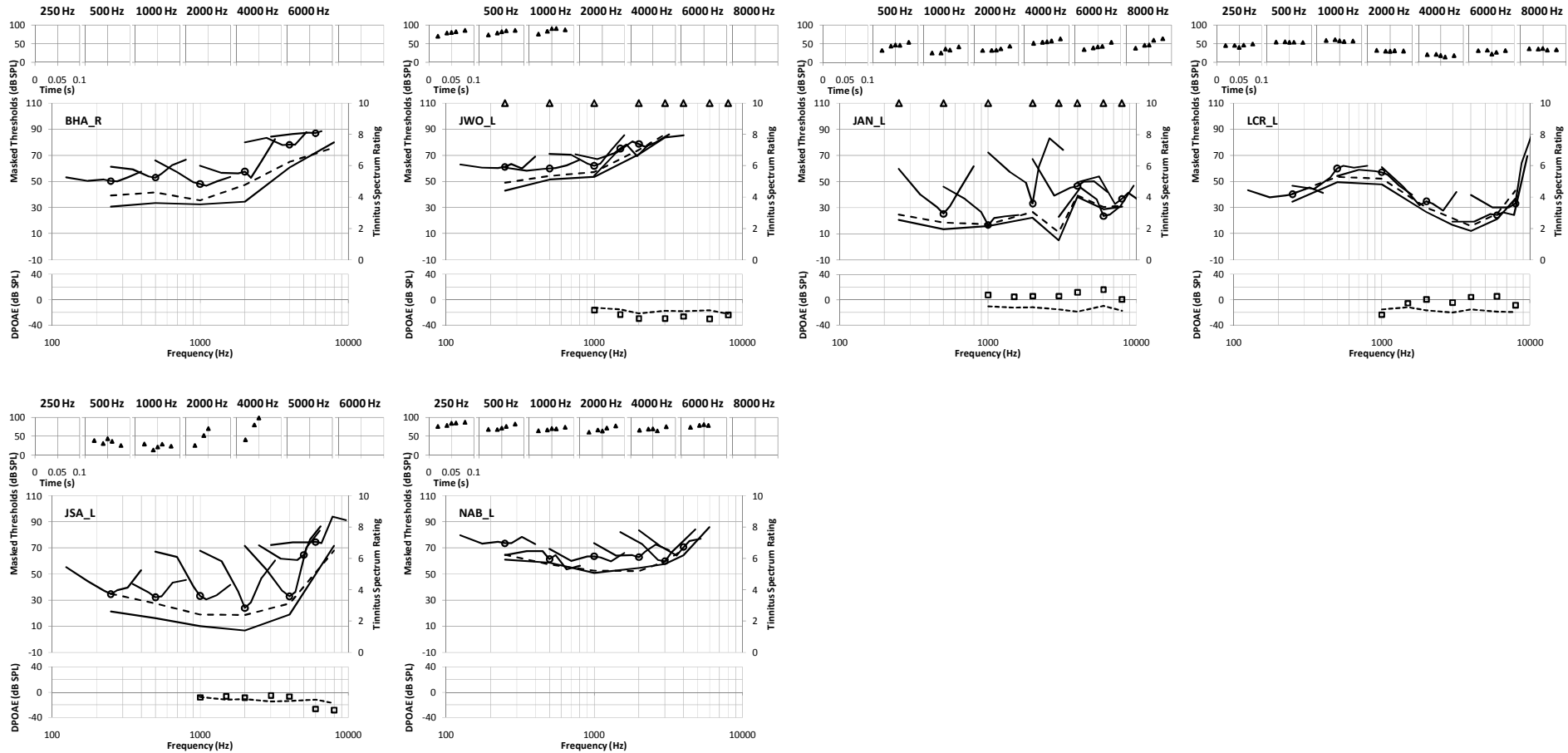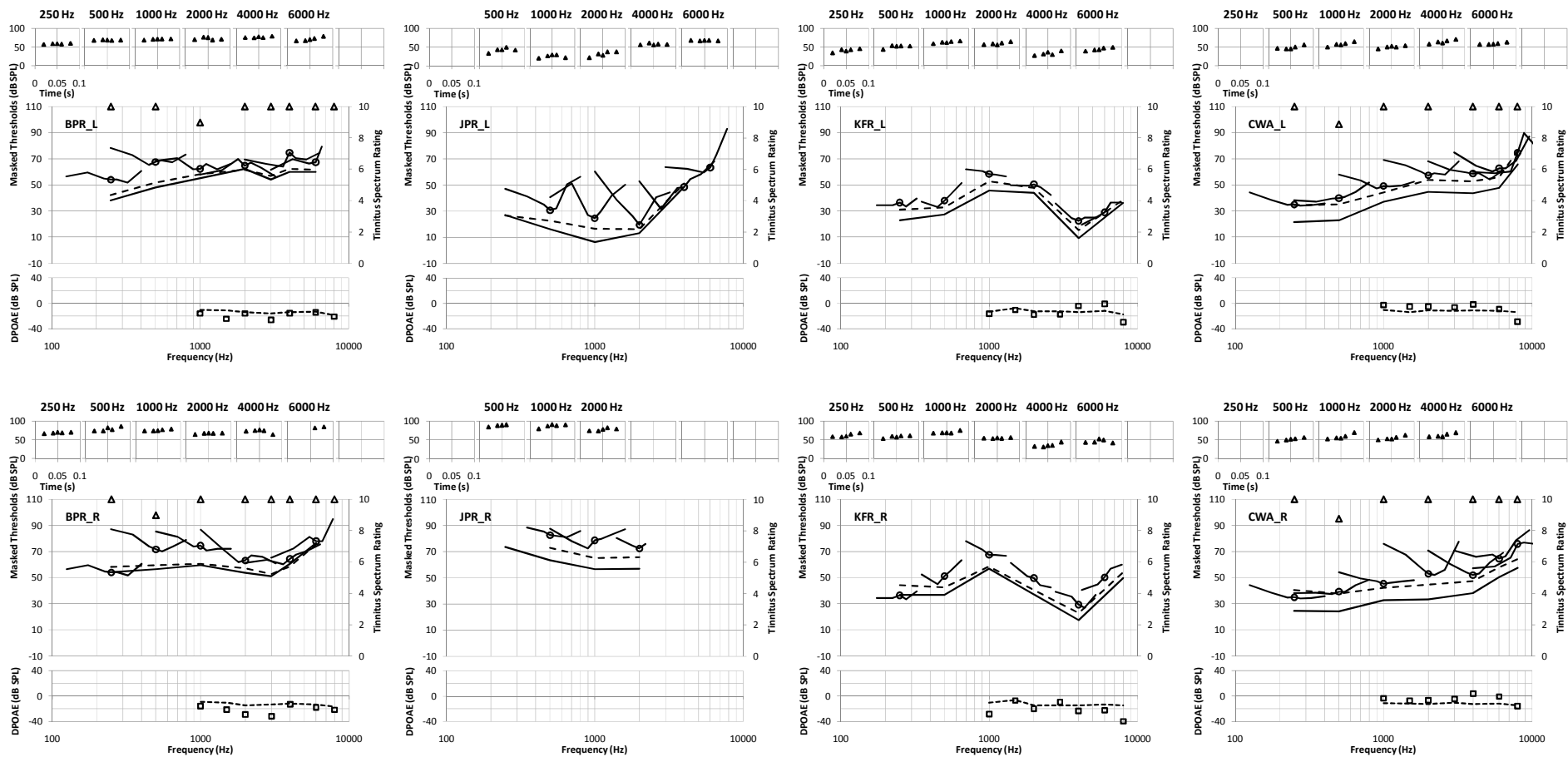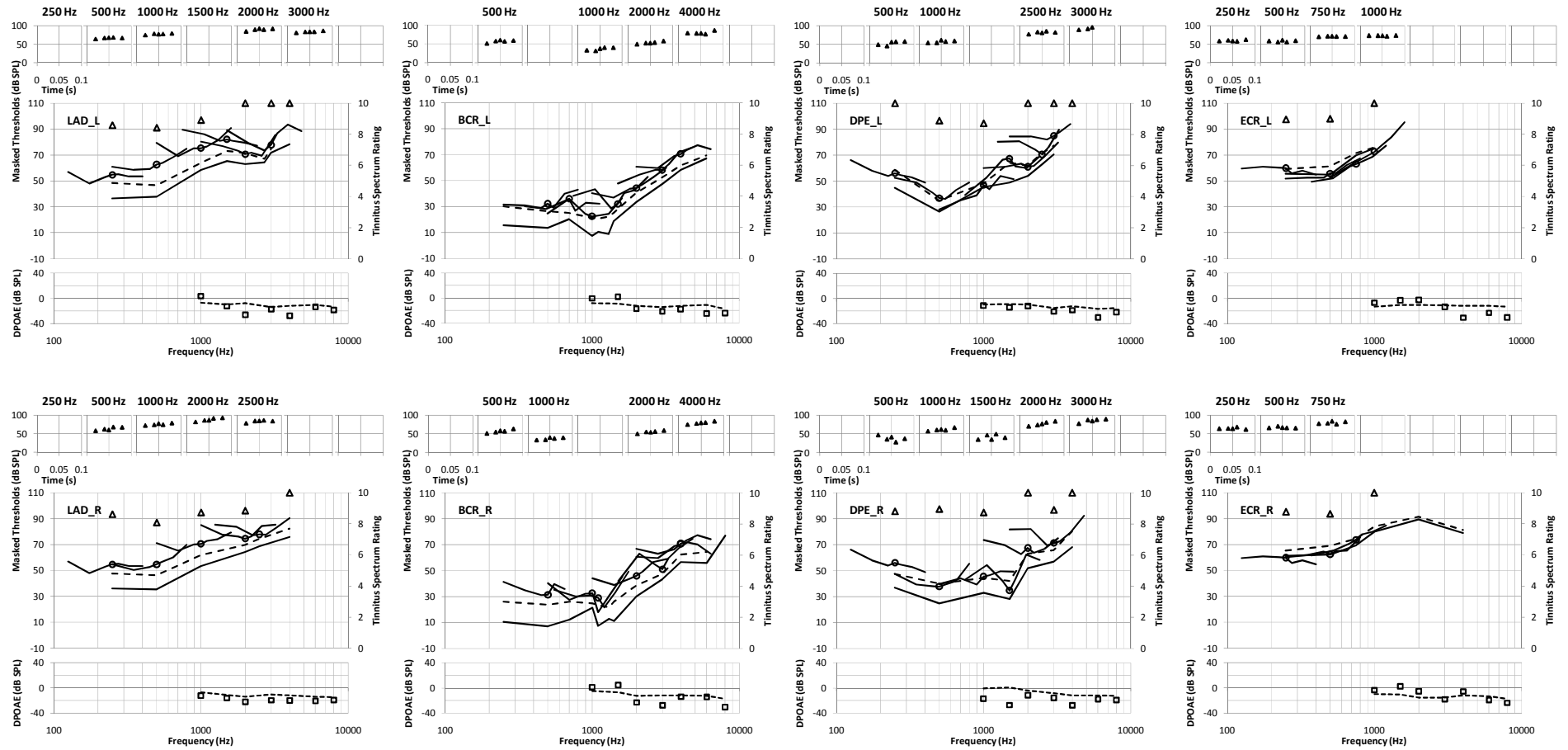
No Tinnitus, Hearing-Impaired

No Tinnitus, Hearing-Impaired

Tinnitus, Hearing-Impaired
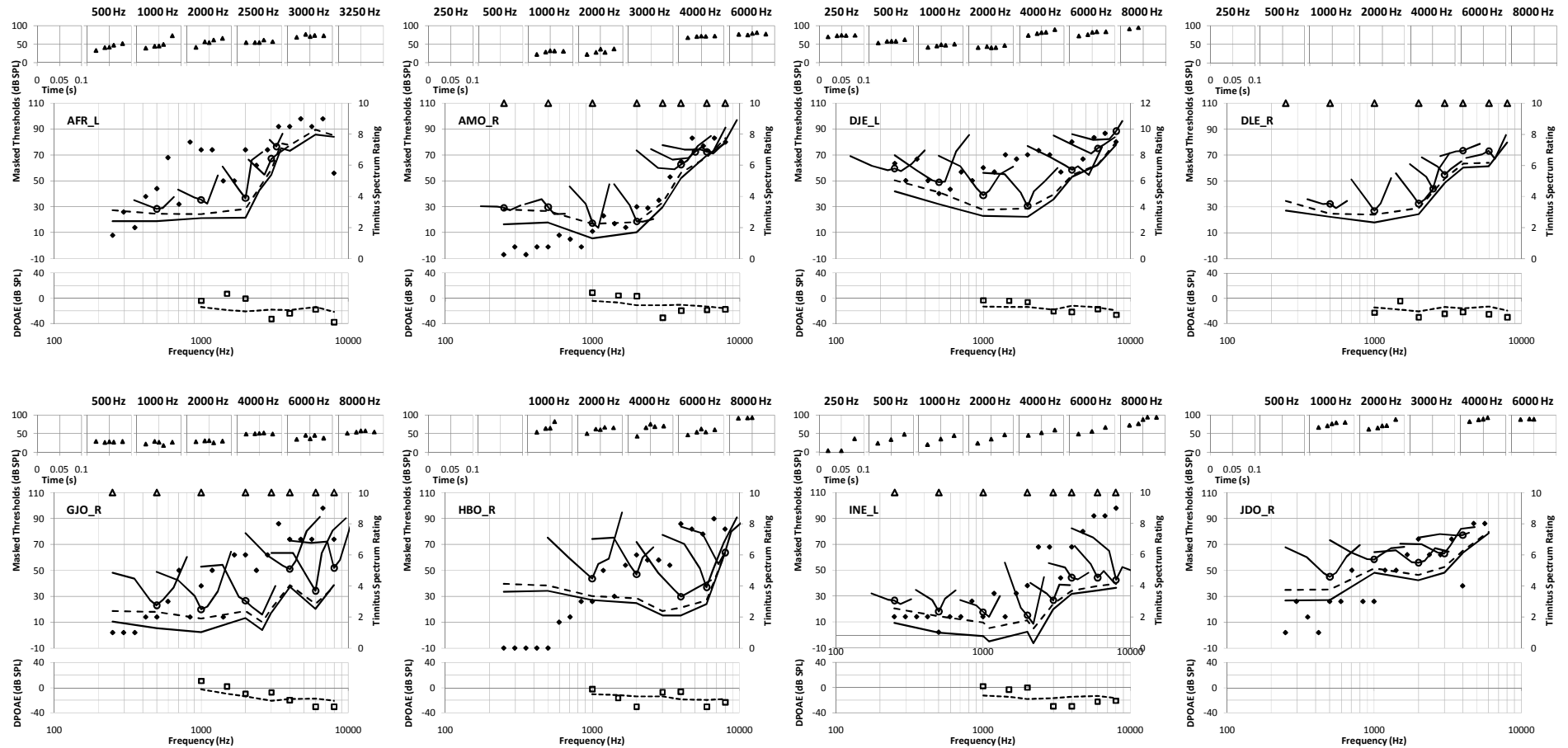
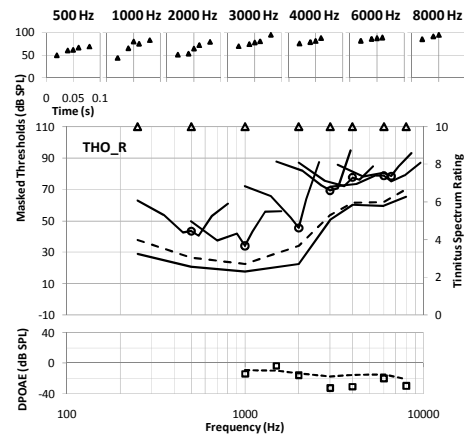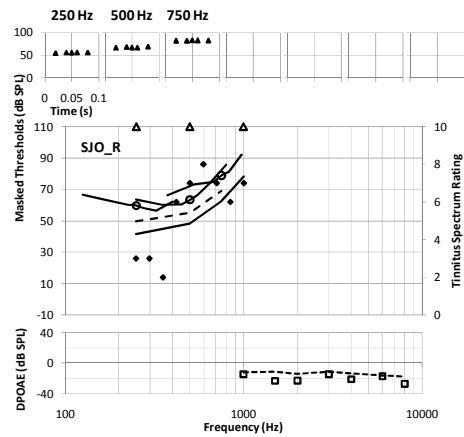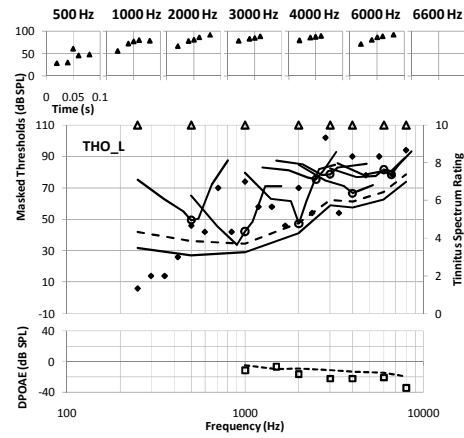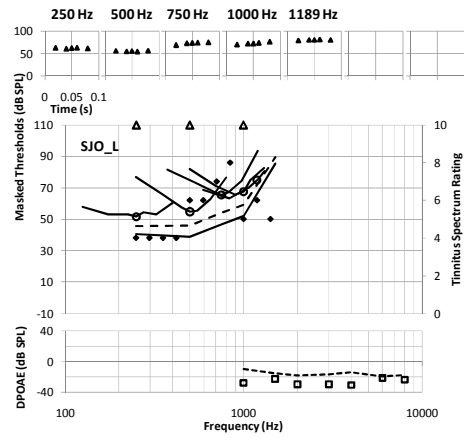# Tinnitus, Hearing-Impaired
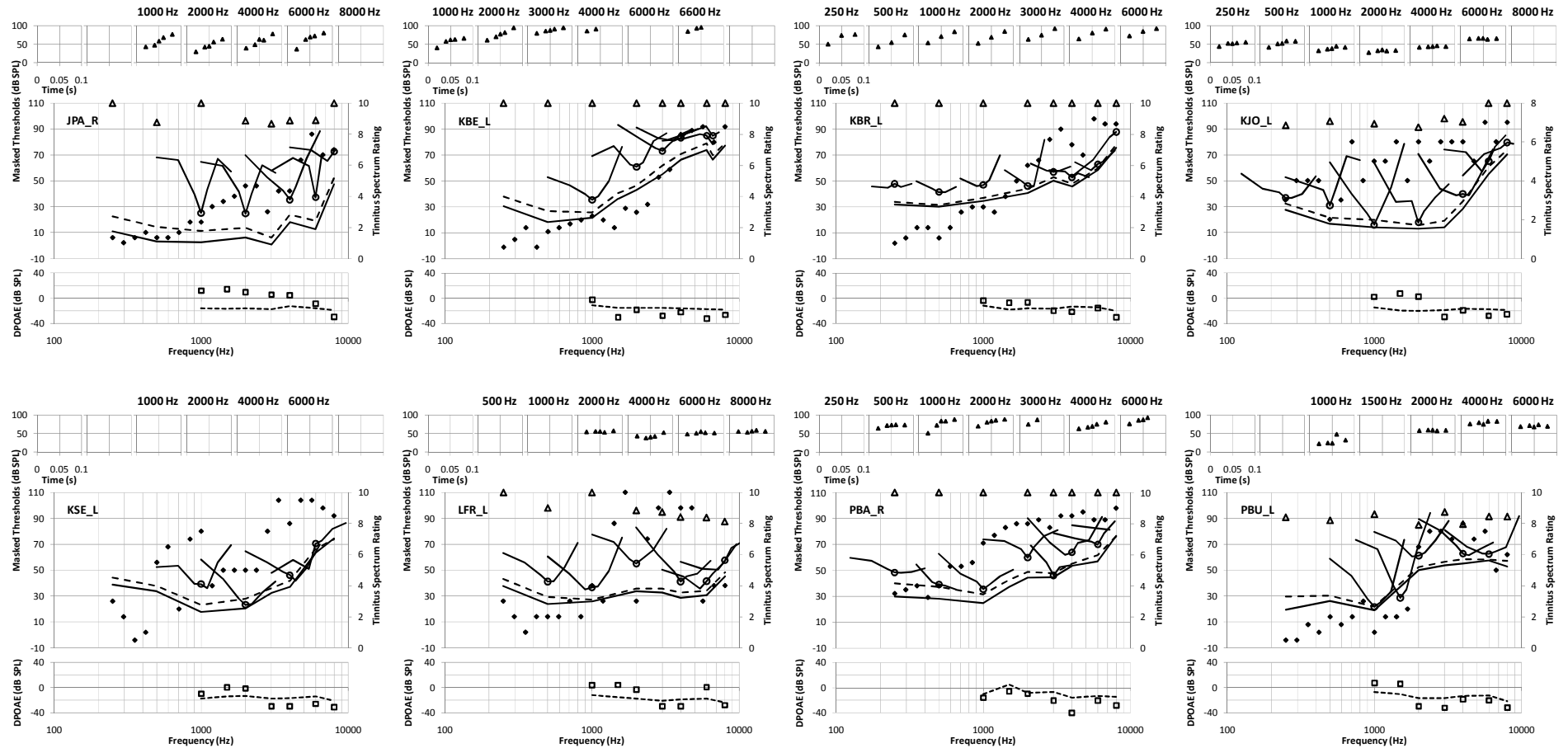
Tinnitus, Hearing-Impaired

Tinnitus, Hearing-Impaired

Tinnitus, Hearing-Impaired

H) Normal-hearing with tinnitus

This section studies the occurrence of tinnitus in individuals with clinically normal-hearing. Normal-hearing people with tinnitus were included in the initial study design to investigate the presence of subtle cochlear anomalies that may not be so obvious using standard clinical measurements. Weisz et al. (2006) first suggested the presence of deafferentation in people with normal-hearing who also have tinnitus. They tested this hypothesis by using the Threshold Equalising Noise (TEN) method, first devised by Moore et al. (2000) to identify inner hair cell defects. They observed that their normal-hearing participants had a poorer pitch scaling ability and that their tinnitus percept coincided with frequency regions identified 'dead regions' in the TEN method.

However, we were unable to replicate the findings by Weisz et al. (2006) because the final number of participants tested in this thesis, for this group, was too small. Some of the participants, who initially thought they had normal-hearing, were found to have impairment at the high frequencies and were thus relocated to the hearing-impaired group. Others did not have a permanent sensation of tinnitus (spontaneous bursts lasting only a few minutes) and these will be introduced separately in this chapter. Hearing profiles of all the participants introduced in this chapter were obtained using the methods detailed in Chapter 3. These included measures of absolute thresholds, frequency selectivity, compression, distortion products otoacoustic emissions, uncomfortable loudness levels and the Tinnitus Spectrum. In some cases, bilateral measurements were possible where subjects were willing to give their consent for extra testing.

Normal-hearing with permanent tinnitus

Only two individuals (JFI and ATY) were allocated to this group. Both of these individuals had clinically normal-hearing and their absolute thresholds did not exceed 20 dB SPL above the average normal thresholds between 250 Hz to 8000 Hz.
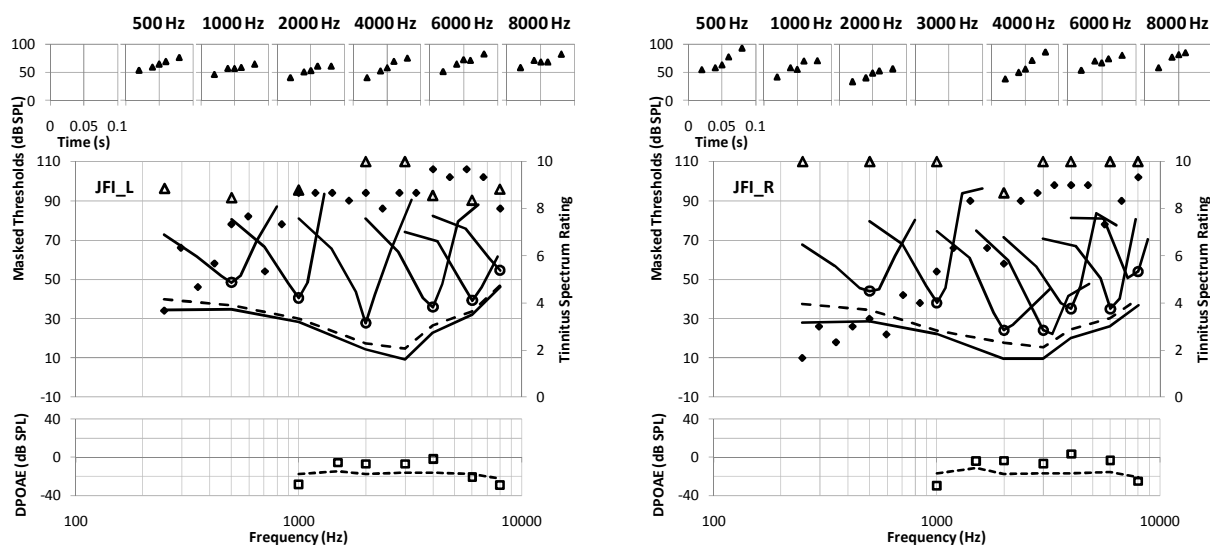

Figure H.1: JFI's hearing profile (left and right). JFI had clinically normal-hearing and permanent tinnitus. Top panel shows the Temporal Masking Curves (triangles) that estimate the amount of compression present. The main body of the Hearing Profile shows the absolute thresholds (250 msec in solid line, 16 msec in dashed line), Iso-Forward Masking Contours that estimate frequency selectivity (solid line with probe frequency identified by a circle), the uncomfortable loudness levels (open triangles) and the Tinnitus Spectrum (solid diamonds). The bottom panel shows the distortion product otoacoustic emissions (open squares) with the noise level indicated by dashed lines.

JFI was a 67-year-old retired office worker without any known history of excessive noise exposure. JFI perceived constant tinnitus in both ears that sounded like 'high-pitched static electricity'. When JFI experiences vertigo, the tinnitus makes a continuous 'bell' sound. JFI had also reported the presence of spondylosis between the 4th and 5th vertebra. This refers to a sense of weakness between the joints, which is a form of degenerative osteoarthritis. JFI also

reported that the perception of tinnitus decreases by up to 50% when performing neck flexion (slow nodding motion). However, the perception of tinnitus was worsened by 50% when performing neck extensions (forward/ backward motion). JFI had a Tinnitus Handicap Inventory (THI) score of 20 (Mild). JFI had good frequency selectivity, strong presence of compression and recordable DPOAEs, all of which suggested good outer hair cell behaviour.
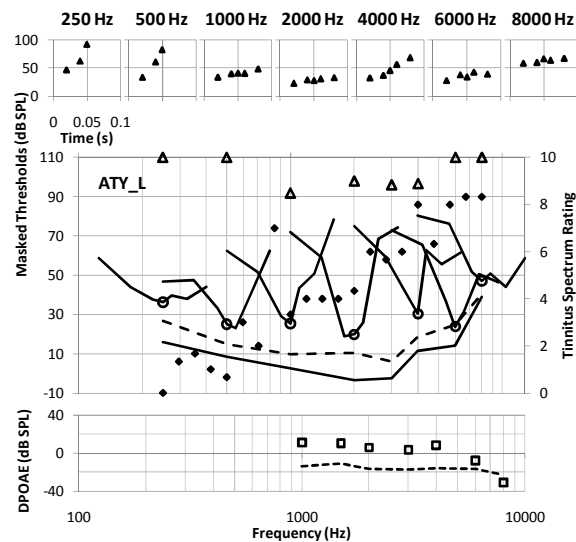

Figure H.2: ATY's left hearing profile. Descriptions are as in Figure H.1.

ATY was a 46-year-old office worker who used to be an electrical engineer but has worked in an office environment for the past 10 years. In ATY's case, constant tinnitus was perceived at 'the back of the head'. The tinnitus sounded like a 'high-pitch whistle', which was very similar to a cathode-ray tube switching on, or to a self-reported frequency of 25 kHz. ATY reported frequent grinding of teeth (possible somatosensory dysfunction, see Section 2.4), but his dentist had not indicated the severity of this condition. When asked to clench both sides of the jaw, ATY reported that the tinnitus doubled in volume (louder) that was slightly more prominent on the left side. ATY reported a THI score of 10 (Slight). ATY also had good frequency

selectivity, strong presence of compression and recordable DPOAEs, which suggest good outer hair cell function.

It is not possible to draw firm conclusions on the cause of the perceived tinnitus that is suspected to trigger the perception of tinnitus in these two people as they have normal-hearing up to 8000 Hz. The high ratings on the Tinnitus Spectrum did not coincide with any sign of impairment. Both participants report somatic conditions that may be associated with tinnitus. It is also possible that damage to their hearing organs is present in the untested regions beyond 8000 Hz, or they may have other non-auditory forms of tinnitus.

Normal-hearing with temporary tinnitus

Three individuals were allocated to this group (JSI, KMA and MLA). All had clinically normal-hearing and their absolute thresholds between 250 Hz and 8000 Hz were within 20 dB SPL of the average normal thresholds. All the participants in this group report having *temporary*, spontaneous bursts of tinnitus that only last a few minutes. The Tinnitus Spectrum had to be done by recalling the pitch of the tinnitus from memory.
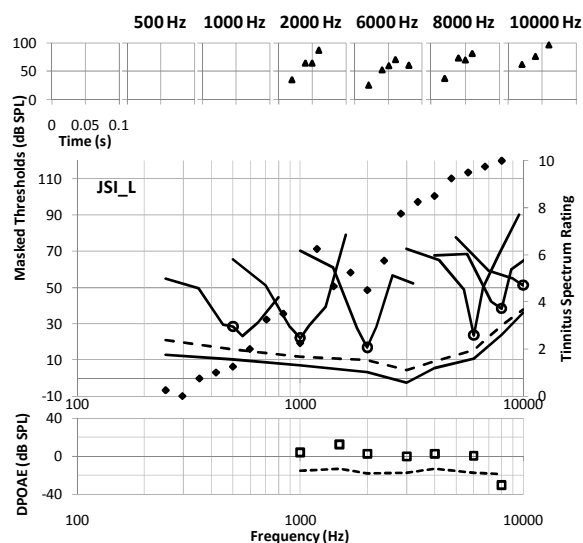

Figure H.3: JSI's left hearing profile. Descriptions are as in Figure H.1.

JSI was a 48-year-old office worker without any known history of excessive noise exposure. JSI had indications of bony growth in the ear canal, possibly due to long-term snorkelling and diving in cold water in the teenage years. JSI perceives tinnitus in both ears on occasion. The tinnitus is reported to have two elements; a high-pitched 'cicada' sound and an intermittent 'low rumbling of an engine in a distance'. JSI's perception of tinnitus sometimes lasted a few minutes and it is easily ignored by performing other tasks. JSI had a self-reported jaw asymmetry, but no knowledge of active grinding of the teeth. JSI reported that clenching the right side of the jaw sometimes changes the tone of the tinnitus. JSI has a THI score of 12 (Slight). JSI's hearing profile suggested that he had good outer hair cell function.
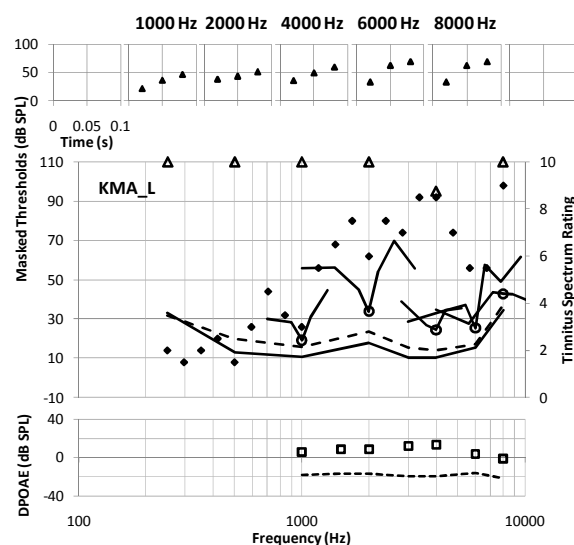

Figure H.4: KMA's left hearing profile. Descriptions are as in Figure H.1.

KMA was a 43-year-old office worker without any known history of excessive noise exposure. KMA had occasional tinnitus in only the left ear that does not last longer than 1 minute. On occasion, the tinnitus sounded like a sharp 'dial tone'. KMA was involved in a car accident 26 years ago, and suffered whiplash. KMA reported grinding of teeth, asymmetric jaw,

frequent headaches, tiredness and hearing clicking sounds when chewing. KMA also had an underactive thyroid and was on medication for the condition. KMA was asked to perform the tasks on the Tinnitus Modulation Manoeuvre Checklist when the tinnitus was present, but did not report any change in pitch or loudness while doing the task. KMA had a THI score of 10 (Slight). KMA's hearing profile suggested the presence of early collapse of the IFMCs (4000 Hz, 6000 Hz and 8000 Hz) that was also in the region where slight intolerance to loud sounds was perceived. This collapse of the IFMCs was previously not seen in people with normal-hearing and without tinnitus. However, measures of compression (using the TMC method) were normal within the same frequency region. One could speculate lack of attentiveness to the task as a possible explanation for the observation. However, these measurements were repeated over 3 runs and the same observations were made in each run. Normal DPOAE responses were present across all frequencies measured. The high ratings on the Tinnitus Spectrum occurred around 3000 Hz and 8000 Hz.
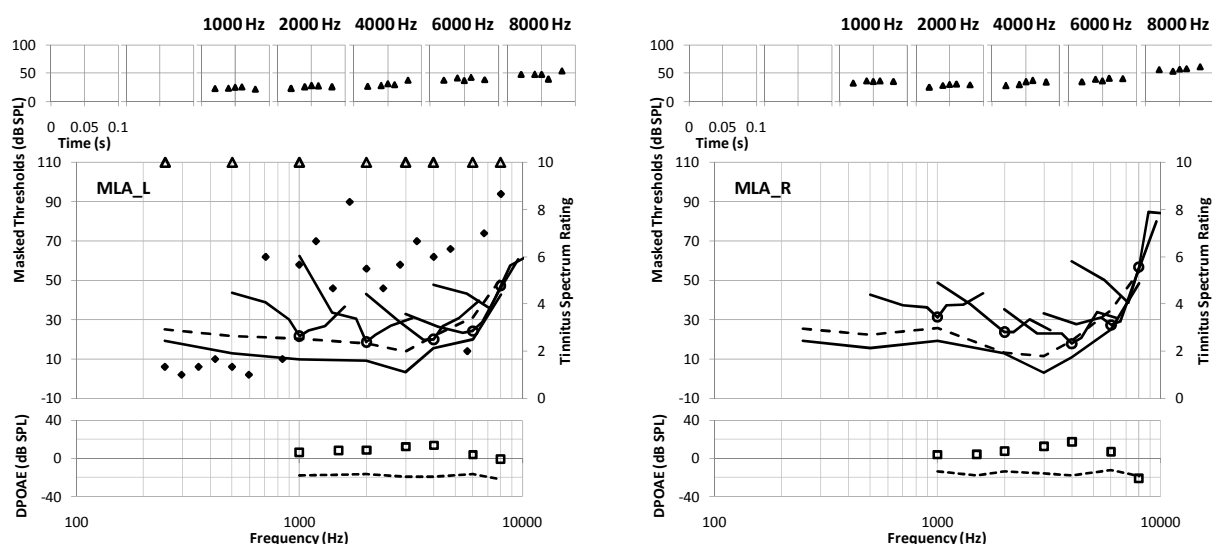

Figure 0.2: MLA's left and right hearing profiles. Descriptions are as in Figure .

MLA was a 56-year-old full time homemaker. MLA has non-pathological tinnitus only on the left ear. Tinnitus was reported to 'feel' spasmodic and intense, and sounded like 'Morse code'. There were two elements to MLA's tinnitus; a high-pitched 'humming', 'buzzing', almost mechanical sound and a low-pitched 'hum' that is constant and does not change in quality. MLA perceives the tinnitus at least once a day. MLA reported frequent headaches and grinding of teeth at night. MLA did not report any change to the pitch or loudness of the tinnitus when performing the tasks in the Tinnitus Modulation Manoeuvre Checklist. MLA had comparatively broader IFMCs and shallower TMC slopes when compared to the normal-hearing population. It is possible that the shallow TMCs were a consequence of masker measurements made below the compression threshold of 30 - 40 dB SPL. If the masker used does not reach the compression threshold, then the TMC slope would reflect the portion of the linear portion of the input/ output function, and hence the shallow slope. However, for the probe levels were set at 10 dB SL, which would allow the masker to reach the compression threshold. Systemic measurement error due to fatigue or inattentiveness could be speculated if a portion of the IFMCs were inconsistent with the observations for a normal-hearing profile (as in the previous case, KMA). However, the broadening of the IFMCs and shallow TMCs were apparent across all frequencies and in both ears. Normal DPOAE responses were present at all frequencies tested and no apparent discomfort to loud sounds were found. High ratings on the Tinnitus Spectrum occurred close to 2000 Hz and 8000 Hz.

In summary, the participants with normal-hearing that were discussed in this chapter did not have any apparent abnormalities that were specific to frequency regions where their own tinnitus was perceived. Some abnormalities in the hearing profiles, however, were uncovered, but due to the small numbers of participants in this group, it is not possible to speculate if these were due to systemic measurement errors or unknown inner ear

abnormalities. Another common factor in this group is the considerable amount of somatic conditions that may be associated with tinnitus. Unfortunately, due to the presence of possible mixed triggers of tinnitus, the exact site of damage responsible for triggering tinnitus cannot be determined.

I) Other conditions associated with tinnitus

This chapter consist of hearing profiles of individuals with tinnitus that may be triggered by pathological or non-auditory insults. These include participants in an early stage of Ménière's Disease (DBR), possible tensor tympani impairment (JTH) and repetitive strain injury (LBR). These participants were considered separately from the main analyses in order to exclude mixed triggers for tinnitus.
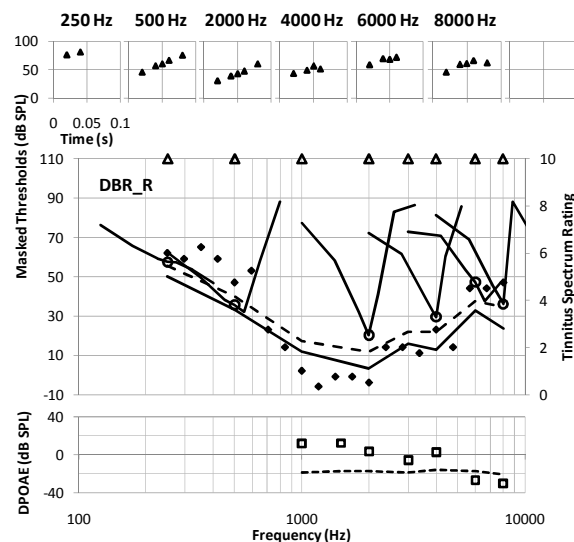

Early stages of Ménière's Disease

Figure I.1: DBR's right hearing profile. Descriptions are as in Figure H.1.

DBR was a 43-year-old musician who also worked in the construction industry. DBR reported sensations of pressure ('blocked') in the right ear and was diagnosed with early stages of Ménière's Disease. The low-frequency hearing loss, presence of self-reported fluctuation in hearing and feeling of fullness in the ear are all indications of Ménière's Disease. Absolute thresholds in the left ear were within normal limits and did not have any indications of abnormal pressure sensations. DBR had occasional tinnitus that was only present in the right

ear and had two distinct qualities. DBR reported that the tinnitus had a very high-pitched tone, which was similar to the tone present 'when switching the television or a megaphone off'. In addition, a low-pitched tone was present in the tinnitus. The action of coupling the hand to the right ear produced distorted sounds similar to 'hearing the sea with a seashell'. DBR reported grinding of the teeth and also hears clicking sounds when chewing or opening the mouth.

Certain tasks on the Tinnitus Modulation Manoeuvre Checklist made the tinnitus slightly louder. These tasks included right gaze (+20%), up gaze (+10% to +15%), up-right gaze (+5%), raising eyebrow (+5%), closing eye tightly (+10%) and smiling widely (+10%). Right lateral flexion of the neck made the tinnitus slightly quieter (-5%). DBR had a THI score of 34.

The actual cause of Ménière's Disease is unknown, though the majority consensus is the presence of endolymphatic hydrops (excess fluid) within the inner ear (Merchant et al., 2005). This in turn, has been suggested to cause loss of outer and inner hair cells and spiral ganglion cells (at the apical turn), as well as further degeneration throughout the Organ of Corti (Nadol et al., 1995).

The hearing profile showed raised thresholds at low frequency, which is consistent with pathological Ménière's Disease. The IFMCs in this region was raised, but retained its sharp V-shape, which suggests good frequency selectivity. TMCs in this region were steep, consistent with the possibility of functional outer hair cells in the frequency region.

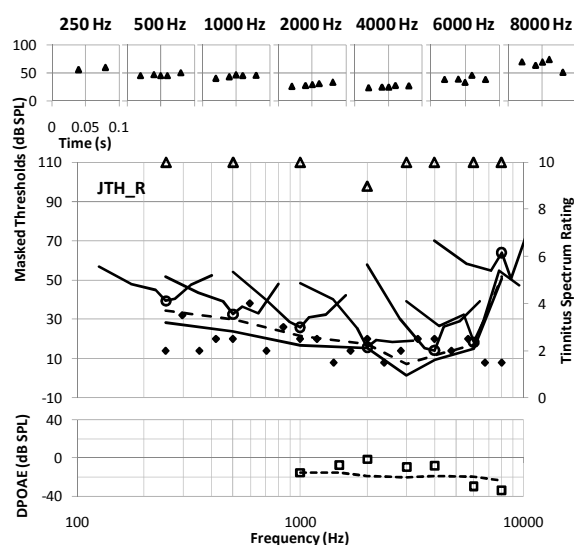**Tensor Tympani Impairment**

Figure I.2: JTH's right hearing profile. Descriptions are as in Figure H.1.

JTH was a 63-year-old dentist. JTH was referred to the study with suspected tensor tympani abnormalities. Tinnitus was only perceived occasionally, but always on the right ear. The tinnitus lasted between 30 seconds to 10 minutes and sounded like 'the fog horn on the Queen Mary'. JTH also reported that the tinnitus was more of a vibration or a sensation rather than a sound or a tone. The tinnitus was matched to tones between 50 Hz to 100 Hz. JTH did not report any abnormalities with the jaw. JTH had a THI score of 8.

Contractions of the tensor tympani muscle have been suggested to be between 30 to 50 contractions per second. Severing of the tensor tympani has been observed to relieve the presence of tinnitus (Hamblen-Thomas, 1937). Tensor tympani impairment has no known detrimental effect on cochlear function. However, the hearing profile showed broad IFMCs and shallow TMCs, which suggest impaired outer hair cell function. DPOAE responses were normal up to 6000 Hz.
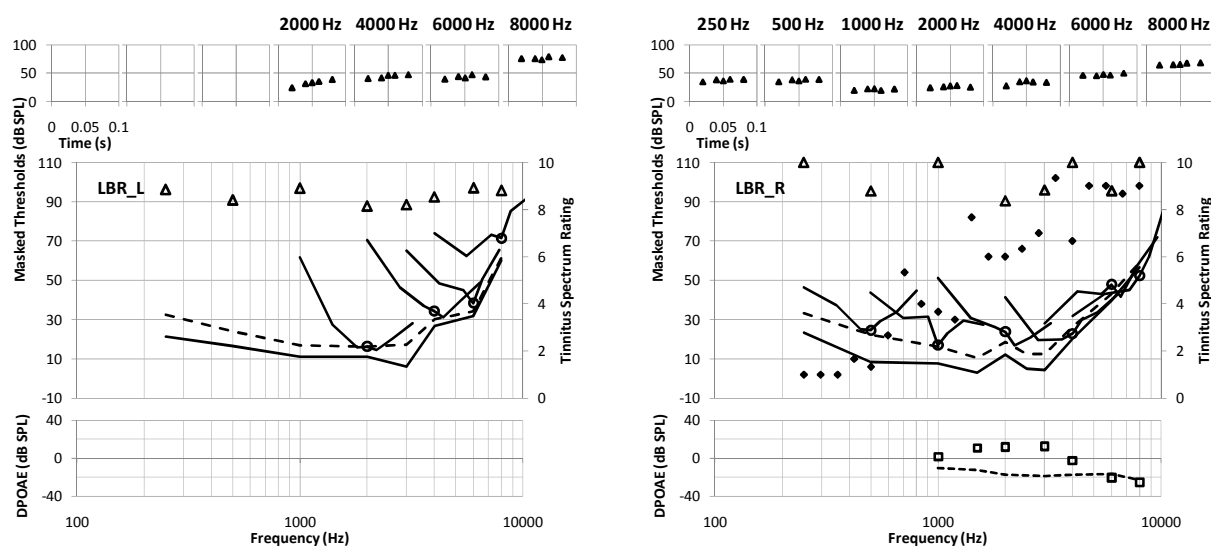
Repetitive Strain Injury

Figure I.3: LBR's right hearing profile. Descriptions are as in Figure H.1.

LBR was a 52-year-old office worker without any known history of excessive noise exposure. LBR reported spontaneous bouts of tinnitus that only mostly in the right ear, and seldom in the left ear. The tinnitus could last up to a few hours and may have a rushing sensation, which is an indication that the tinnitus will get louder, which is normally followed by migraines. LBR did not report abnormal jaw problems, but reported to be diagnosed with Repetitive Strain Injury along the right side of the neck, which constantly feels taut, painful and stiff. LBR is able to 'switch on' the tinnitus by rotating the neck towards the right in a certain manner. LBR is also suspected to have occipital neuralgia which can be attributed to nerve damage behind the eyes. Some tasks on the Tinnitus Modulation Manoeuvre Checklist made the tinnitus louder; tight eyelid closure (+40%), lip pursing (+40%), blowing up the cheeks (+40%), neck extension (+40%), lateral flexion of the neck toward the left produces a clicking sound behind the left ear, rotation of the head in an anticlockwise direction (+40%). LBR has a THI score of 28.

Injuries to the head and neck regions have been reported together with the presence with tinnitus. The perception of tinnitus is often located at the ipsilateral region of the injury, it is still unknown what exact somatic interactions trigger the perception of tinnitus, although Levine (1999) suggests that disinhibition at the level of the dorsal cochlea nucleus, due to trauma to the somatic system, as a possibility.

LBR's hearing profile was strikingly different for the left and right ears. The left ear that was less affected with tinnitus had clearly better frequency selectivity and steeper measures of compression than the right ear, where tinnitus was perceived. It may be possible that this difference reflects higher unknown processes that are not of cochlear origin.