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Examining the Roles of Residuals Under an Adaptation Level Theory Model for Tinnitus Perception

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Abstract

**Background:** Tinnitus is the perception of sound in the absence of sound in the environment (1-4). The precise mechanisms giving rise to tinnitus perception and distress are still not fully known. The Adaptation Level Theory (ALT) model of tinnitus (5, 6) is an ecological framework which takes a holistic approach to understanding tinnitus and its complexity, in which tinnitus magnitude estimates are based on interactions between the focal component (tinnitus), contextual component (any background noise or applied sounds), and residual components (individual cognitive and behavioural characteristics).

**Aim:** To empirically explore the influence and strength of individual residual factors under a novel Adaptation Level Theory (ALT) model of tinnitus perception. Personality traits, emotion and prediction/anticipation of sounds were residuals examined.

**Methods:** Seven studies were undertaken as part of this doctoral thesis: 1) A scoping review investigated key personality traits relevant to tinnitus, and the relationship between affective disorders and tinnitus. 2) A web-based survey was administered to 154 individuals with tinnitus and 61 age, gender and hearing level-matched non-tinnitus controls. The survey measured four key self-reported personality traits (social closeness, stress reaction, alienation and self-control), tinnitus characteristics and hearing handicap. 3) A behavioural experiment (N=22) introduced short-term emotional stimuli, differing along valence and arousal dimensions, and measured tinnitus loudness and annoyance characteristics. Stimuli were presented in two modalities: auditory and visual. 4) A comprehensive narrative synthesis of current research assessed the feasibility of a relationship between auditory memory, predictive coding and tinnitus generation. 5) A short-term adaptation experiment (N=23) and two-week feasibility trial (N=7) compared the effect of predictable and unpredictable amplitude-modulated computer surf sound on tinnitus loudness and annoyance characteristics. 6) An electroencephalography (EEG) study that compared mean ERP amplitudes and oscillatory band activity in response to tone deviants and tone omissions (at the pitch of tinnitus) between individuals with tinnitus (N=16) and hearing-level matched controls (N=14). 7) A randomized tinnitus sound therapy clinical trial (N=18) was conducted comparing the effectiveness of nature sounds with neutral broadband noise. Multiple experimental outcomes relating to tinnitus, emotion, attention and psychological state were
measured at three time points: at sound fitting, 4 weeks after administration and 8 weeks after administration.

**Results:** 1) The scoping review concluded personality traits to have a consistent association with the distress experienced by adult tinnitus help-seekers, and help-seekers were also more likely to experience anxiety and depression symptoms and/or disorders. Limitations present in current research were lack of appropriately controlled comparisons when assessing personality trait profiles of tinnitus sufferers and non-tinnitus individuals. 2) Tinnitus sufferers displayed higher levels of stress reaction, lower social closeness, lower self-control and higher alienation than the control group in the web-based survey. 3) In the behavioural emotion experiment, low valence (unpleasant) auditory stimuli led to higher subjective tinnitus loudness ratings in males and females and higher subjective distress ratings in males only. Visual emotional stimuli did not have an effect on tinnitus characteristics. 4) The narrative review provided theoretical support and indirect electrophysiological evidence for continuous prediction errors generated within the auditory system driving tinnitus perception and distress, as well as eliciting global disruptions to attention and working memory. 5) Both short-term Unpredictable and Predictable sound administration led to a decrease in tinnitus loudness in the adaptation experiment, however, only Unpredictable sound lowered tinnitus distress ratings. 6) A larger N1c waveform was elicited in the absence of any tone deviation within the left primary auditory cortex of tinnitus participants for the EEG study. Abnormal N1c waveform growth was present across levels of deviant conditions for the tinnitus group. There was limited evidence to support the Thalamocortical Dysrhythmia hypothesis of greater theta and gamma activity present among individuals with tinnitus. A role for attention and auditory scene analysis in driving tinnitus perception and salience was supported. No differences were present between groups for tone omissions. Different levels of activity between tinnitus and control groups were observed in regions corresponding to attentional as well as limbic networks. 7) The administration of sound therapy led to significant reduction in tinnitus impact over 8 weeks; this effect was largely due to BBN sound therapy which resulted in significantly greater reduction of tinnitus impact compared to nature sounds. The positive effect of sound on tinnitus was supported by secondary tinnitus and psychological-related outcome measures, but not interviews. BBN sound resulted in an increase in loudness level matches needed to match tinnitus; there was minimal change in loudness level matches for nature sounds. There were indications of individual preferences and individual outcome effects observed. The presence of tinnitus subgroups was apparent in terms of which sound...
was most favoured, which sound had the most benefit, as well as in how sound-tinnitus interactions occurred as time progressed.

**Conclusions:** Personality traits, emotion and prediction all play a significant role as residual factors under the ALT model to shape final tinnitus perception and experience as well as in influencing response of tinnitus to introduction of external sound introduction. Overall, tinnitus magnitude appears to increase with high stress reaction, low social closeness, low self-control and high alienation personality trait levels, as well as by the introduction of unpleasant auditory stimuli. In contrast, the presence of sound therapy stimuli decreases tinnitus magnitude and demonstrates psychological benefit over time. This thesis provides some empirical support for the ALT model of tinnitus. Further research is needed to examine attention as a weighting factor, develop clinically useful indicators of ideal sound therapy levels under the ALT framework, as well as customize therapeutic sound to tailor for individual residual levels, needs and preferences over time. Development of computational models based on the ALT which integrate residual factors, weighting factors and tinnitus-external sound interactions may be useful for delineating subgroups and predicting how an individual might respond to potential treatments. The findings from this thesis can form a basic computational template to build-on.
Dedication

Matha, Pitha, Guru, Deivam
(My Mother, My Father, My Teacher, My God)
To each, for guiding me along the path of life
For teaching me purpose and helping me continuously seek knowledge and truth

Santosh & Varna
For your unconditional love, support and patience
For being my inspiration, my rock and my fortress

Family & Friends
Those with me today and those much missed
For surrounding me with warmth, spirit and cheer
For shining down on me from heaven everyday
For dear Appayya
“She will break down the walls of University”
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Thank you to my participants, you were a truly lovely group of people whose comments, well-wishes and feedback encouraged me to strive towards future research in tinnitus. Your time and interest in my study is much appreciated.

Thank you Amma, Appa and Thamba for all that you have done for me and which I cannot possibly even start to repay. To say that you have significantly gone out of your way to make me comfortable, well-fed and happy while I undertook this journey will be an understatement. I am thankful to have you all by my side. Thank you for believing in me enough to let me choose my path; I hope that you are proud of the progress made.

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Figure 33. Grand averages of the statistical maps comparing oscillatory band activity between tinnitus sufferers and controls for the frequency-7 condition (P2 time window). The brighter colours indicate higher values of the t-statistic according to the colour scale. Blue indicates regions which show greater activation in the tinnitus group compared to controls; red indicates regions with greater activation in controls compared to the tinnitus group. Analyses showed greater cortical sources in the precentral gyrus (BA = 6) for the tinnitus group than controls.

Figure 34. Grand average of the statistical maps comparing oscillatory band activity between tinnitus sufferers and controls for the frequency-7 condition. The brighter colours indicate higher values of the t-statistic according to the colour scale. Analysis showed significant lower sources of beta-2 (18.5–21 Hz) rhythms in the right inferior occipital gyrus (BA 19) in the tinnitus group.

Figure 35. Unweighted power spectrum density plots (dB SPL/Hz) showing relative signal strength across frequencies using an artificial ear for the three nature sounds used in the study for Unpredictable sound therapy (Surf (A), Cicadas/Farm Sounds (B), Rain (C)) and BBN for Predictable sound therapy (D). A G.R.A.S.Artificial Ear Type 43AC coupler was used and sounds were played directly through the MP3 and Panasonic earphones. Recordings used a National Instruments PXI-4461 sound card and LabVIEW 8.0 was used to analyse the sounds.

Figure 36. Protocol for data collection. Multiple outcome measurements were taken at the following time points: 1st sound fitting (Baseline), and 4 weeks and 8 weeks after first fitting while the sound was being used. A washout period of 3 weeks followed in which no sound was administered. Multiple outcome measurements were then taken at the following time points: 2st sound fitting (Baseline), and 4 weeks and 8 weeks after second fitting while the sound was being used.

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Figure 38. Annoyance ratings growth curves of each therapy sound (Rain (A), Cicadas on Farm (B), Beach (C), BBN (D)) as a function of noise level (% between hearing threshold and minimum masking level for tinnitus).
level for tinnitus). Annoyance functions show decreases in tinnitus annoyance (solid black line) and increases in sound annoyance (solid grey line) as a function of sound level. The equal annoyance point (square symbol) defines the sound level at which both tinnitus and sounds were of equal perceived annoyance (point of intersection between tinnitus annoyance and sound annoyance functions). Figure 39. Average valence ratings of sound therapy stimuli by participants. Error bars represent +/- one standard error. Figure 40. (A) Individual TFI scores of participants at baseline, at 4 weeks follow-up and at 8 weeks follow-up following administration of BBN and nature sound stimuli. Horizontal lines represent average TFI scores. (B) Average TFI scores of participants at baseline, at 4 weeks follow-up and at 8 weeks follow-up following administration of BBN (black) and nature (grey) sound stimuli. The significant difference is indicated by (*, p<0.05). Error bars represent +/- one standard error. Figure 41. Tinnitus loudness ratings (on a scale of 1-10, where 1 corresponded with very quiet tinnitus and 10 with extremely loud tinnitus) and annoyance ratings (on a scale of 1-10, where 1 corresponded to low in distress and 10 with extremely high distress) of participants at baseline, at 4 weeks follow-up and at 8 weeks follow-up. Significant differences are indicated by (*, p<0.05). Horizontal lines represent average rating scores. Figure 42. Average LLMs (in dB SL) at baseline, at 4 weeks follow-up and at 8 weeks follow-up following administration of BBN and nature sound stimuli. Horizontal lines represent average tinnitus loudness matches (in DB SL). Significant differences are indicated by (*, p<0.05). Error bars represent +/- one standard error. Figure 43. Positive Emotionality and Negative Emotionality scores at baseline, at 4 weeks follow-up and at 8 weeks follow-up. Horizontal lines represent average scores. Significant differences are indicated by (*, p<0.05). Figure 44. Anxiety, depression and stress scores of participants at baseline, 4 weeks follow-up and 8 weeks follow-up. Horizontal lines represent average scores. Significant differences are indicated by (*, p<0.05). Figure 45. Box plot showing minimum, lower quartile (25%), median, upper quartile (75%) and maximum CAB Reaction Time Task response times (ms) of participants at baseline and after 8 weeks administration of nature (white) and BBN (grey) sound stimuli. Figure 46. Box plot showing minimum, lower quartile (25%), median, upper quartile (75%) and maximum CAB Discrimination Time Task response times (ms) of participants at baseline and after 8 weeks administration of nature (white) and BBN (grey) sound stimuli. Figure 47. Changes in outcome measures ((A) tinnitus loudness ratings, (B) tinnitus annoyance ratings, (C) MML, (D) negative emotionality, (E) positive emotionality, (F) anxiety, (G) depression, (H) stress, (I) attention reaction time, (J) attention discrimination time) for each participant following administration of BBN (black) and nature (white) sound stimuli. Figure 48. Perceived effectiveness of sound therapy by participants (benefit, no change or worse) for BBN (black) and nature (grey) sounds at 4 weeks. Figure 49. Perceived effectiveness of sound therapy (benefit, no change or worse) for BBN (black) and nature sounds (grey) at 8 weeks. Figure 50. Average audiometric thresholds (dB HL) of participants for three participant groups: those who preferred the BBN sound at 8 weeks, those who preferred the nature sound at 8 weeks and those who did not have any preference. Figure 51. Conceptualization of current study findings under an adaptation level theory (ALT) framework for tinnitus perception (5). Tinnitus is envisaged as a sensory stimulus with an existing internal adaptation level (AL) which acts as a reference point for all tinnitus-related judgments and is able to be manipulated by context and time. A high tinnitus AL results in tinnitus that is judged by the sufferer as being of high magnitude and/or eliciting high distress. Three key components set the final AL: 1) the focal component/stimuli being attended to (tinnitus), 2) background stimuli, as well as 3) residuals (various psychological and cognitive individual influences, including emotion, personality, past experiences, arousal and level of prediction elicited by sound stimuli). The ‘presence of sound
effect' (red arrows) illustrates steady shifts in AL away from the tinnitus and towards sound therapy stimuli, which can occur by directly increasing the weighting placed on external sound, via attention and auditory streaming shifts. A valence of sound effect increases weighting placed on external sound via the residual pathway. The latter occurs as external sounds provide psychological relief from tinnitus and can counteract tinnitus-related negative emotions, anxiety, stress and depression, thereby creating a facilitating residual effect which reduces tinnitus severity. The ‘predictability difference effect’ (blue arrow) illustrates a potential difference between BBN and nature sounds in terms of the amount of prediction errors elicited; this may also influence the degree of adaptation each sound undergoes over time. Shifts in AL away from tinnitus towards external sound would discontinue upon adaptation of the auditory system to the external sound itself. Auditory system adaptation to BBN and natural sound therapy may occur at different rates. Adaptation to BBN occurs sometime between 4 and 8 weeks after the first introduction of the sound, leading to the need to increase the sound level required to match tinnitus in Loudness Level Matching. There may be small but immediate valence effects, but nature sounds due to their intermittent nature may take longer to reach peak adaptation, such that at 8 weeks no change in Loudness Level Matching may be observed.

Figure 52. The presence of ‘maladaptive’ personality traits – high stress reaction, high alienation, low social closeness and low self-control increase tinnitus AL weighting overall by reducing ‘r’ weighting and increasing ‘p weighting’ of tinnitus.

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Title: Anxiety and Depression, Personality traits relevant to tinnitus: A scoping review. Accepted for publication in International Journal of Audiology, 2015. Content from this paper is included in Chapter 3 of this thesis.

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Title: The personality profile of tinnitus sufferers and a non-tinnitus control group. Accepted for publication in Journal of the American Academy of Audiology, 2016. Content from this paper is included in Chapter 4 of this thesis.

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Title: Examining the short term effects of emotion under an Adaptation Level Theory Model of Tinnitus Perception. Submitted to Hearing Research, 2016. Content from this paper is included in Chapter 5 of this thesis.

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Title: A review of the role of memory and prediction in tinnitus perception. Submitted to The Journal of the American Academy of Audiology, 2016. Content from this paper is included in Chapter 6 of this thesis.

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Please indicate the chapter/section/pages of this thesis that are extracted from a co-authored work and give the title and publication details or details of submission of the co-authored work.

Title: The short-term effects of predictable and unpredictable surf-like sounds on tinnitus adaptation. Submitted to Acta Acustica United with Acustica, 2016. Content from this paper is included in Chapter 7 of this thesis.

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Title: Auditory streaming and prediction in tinnitus sufferers. Submitted to Ear and Hearing; 2016. Content from this paper is included in Chapter 8 of this thesis.

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<tr>
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Chapter 1. Introduction
Tinnitus is the perception of sound in the absence of sound in the environment (1-4). The precise mechanisms giving rise to tinnitus perception and distress are still under study and no single theory of mechanism is universally accepted, although it is now understood to be mostly a consequence of deafferentation of peripheral auditory signals resulting in compensation or inadequate noise reduction in central processing pathways (2, 7-9). Final tinnitus magnitude is thought to result from activity within auditory, personality, emotion, attention and memory networks (5, 6, 10). While tinnitus occurs in 4-32% of the general population depending on definition, only about 15-20% of the tinnitus population experience disruption to quality of life and distress, such as disturbed sleep and concentration, problems with hearing, irritation and annoyance, anxiety and depression (11-13). Hearing loss and hearing-related problems are common risk factors for more debilitating tinnitus (14). Tinnitus prevalence increases significantly with hearing loss (3, 15), especially sensorineural hearing loss and individuals with tinnitus also frequently complain about difficulties associated with hearing (16, 17). Moreover, tinnitus pitch often correlates with the region of greatest hearing loss (or peripheral deafferentation) in an individual (18, 19).

Currently, sound therapy is widely used in several paradigms for tinnitus management. Sound therapy uses external sounds to modify tinnitus perception and/or reactions to it (5, 20-24). External sound may immediately provide relief by masking tinnitus (20, 21); if presented over a longer-term, changes in tinnitus functional networks have also been observed (25-27). Sounds currently used in therapy include broad-band noise (BBN), narrow-band noise (either pitch-matched or unmatched to tinnitus), environmental sounds or music (28-30). Despite its popularity, there is no consensus as to the most appropriate sound parameters for tinnitus therapy, or if the treatment provides independent benefit over psychological effects alone (20, 31, 32). It is likely that the difficulties encountered in identifying useful therapies may also partly result from the homogeneous nature of tinnitus.

Although categorization of patient characteristics have been used to guide focus of treatments (e.g. hearing aids, counselling, use of sound therapy (33)), the selection of sound type based on individual needs does not appear to be widespread or documented. Within a clinical setting it is currently not possible to fully predict how individual variables may affect tinnitus treatment outcomes, and multidisciplinary approaches are often utilized (34, 35) in the hope of finding an approach which best works for an individual. The drawback of taking such an
approach is that it may become time-consuming and dishearten or stress individuals over longer periods of time.

Traditional psychoacoustic models to date have tended to adopt a reductionist approach, focusing on individual perceptual characteristics of tinnitus which can be formally reported and measured, such as pitch and loudness (36-39). It is arguable that this approach is limited in understanding tinnitus, which is a dynamic phenomenon and that does not follow all the rules which apply to external sound (40-42). Searchfield et al. (5) developed an ecological model of tinnitus perception by applying Helson’s (43) ALT theory to magnitude estimates of tinnitus. Tinnitus is conceptualized as an auditory object with an existing adaptation level (AL) (the body’s internal anchor or reference point) (43). This reference point is used for comparing and estimating the magnitude of incoming sensory stimuli, as well as for making perceptual and discriminatory judgements. The ALT model adopts a holistic approach in understanding tinnitus; the final AL is the weighted mean of 3 components: 1) the focal component (tinnitus), 2) contextual stimuli (any background noise or applied sound therapy) and 3) residuals (individual cognitive or behavioural factors such as past experiences, prediction, emotion, personality traits, and physiological arousal). Attention and auditory scene analysis (ASA) processes are weighting factors; the component that is attended to at any point in time will be given greater weighting and have increased influence in setting the internal anchor. An elevated internal tinnitus AL may represent tinnitus that is perceived as being of high magnitude and/or eliciting greater distress. Moreover, the adaptation level is determined by both present and past experiences of a stimulus and is able to change over time (43, 44). Environmental influences on tinnitus may encompass dynamics of the physical environment as well as broader, slow-changing social factors such as an individual’s cultural norms, beliefs, religion, relationships and moral support.

The ALT framework may unify existing physiological (e.g. gain adaptation), psychological (top-down influences on threshold of detection and emotional affect) and psychoacoustic models of tinnitus in order to solve gaps in knowledge about tinnitus. As the model is based on a mathematical formula, it is theoretically possible to calculate optimal parameters or foci for intervention. Empirical investigation of the theoretical ALT model of tinnitus is needed, particularly with regards to which residuals show a relationship with tinnitus, and their systematic interactions with the phantom sound perception.
Residuals examined in this doctoral thesis include personality traits, emotional affect, and previous experiences/memory of the tinnitus and prediction of sound (45). Personality traits define the typical thoughts, actions and behaviours of an individual (46-48); these traits are determined by both genetic and environmental factors (49-52). Personality traits have been described as potential moderators of tinnitus distress (53). Certain ‘maladaptive’ personality residuals under this ALT framework may exist which divert attention and auditory processing resources towards the tinnitus, thus increase its AL weighting.

Emotion defines a specific, affective reaction to a particular event, and is typically of shorter duration than a mood (54). Processing of emotional sound within the brain may involve complex neural interactions between the auditory system and the limbic system (the amygdala, hippocampus and insula) (55, 56). Alterations to the limbic system in chronic tinnitus have been commonly examined in neurophysiological tinnitus models (8, 23, 57-59). The ALT model proposes that certain emotions may prime or shape perception and response to tinnitus via top-down, higher order influences.

Detecting regularities or patterns in incoming sound allows the auditory system to identify objects in complex auditory scenes (60, 61). Moreover, temporal (concerning ‘when’ or onset of a stimulus) and formal regularities (‘what’ or physical features of stimulus) can also be used to determine which future stimuli might occur (62, 63). These predictions ensure that sensory processing is economical and cognitive resources are allocated towards processing of novel stimuli (64-66). Dysfunctional prediction processing may give rise to the phenomenon of tinnitus (7, 67). This hypothesis is compatible with the ALT model that suggests an important role for auditory scene analysis (61, 68-70) in tinnitus.
1.1. Objectives

1. To better understand mechanisms of tinnitus perception and sound therapy.

2. To test the Adaptation Level Theory (ALT) of tinnitus perception.

3. To understand if application of the ALT model to tinnitus could lead to more effective and efficient treatments.
Chapter 2. Literature Review
2.1. Tinnitus Overview

2.1.1 Definition and classification

The term tinnitus originates from the Latin tinnire, which means ‘to ring’ (71). Subjective tinnitus is the involuntary perception of one or more sounds by an individual, in the absence of an external physical source (2, 3, 34, 72-75). It is thus a phantom perception. There has been an upsurge in scientific tinnitus research in the last few decades, following increased clinical observations and more awareness of the phenomenon (34, 73). It is important that tinnitus is distinguished from auditory hallucinations, which are more complex auditory phenomena present in patients with psychosis or schizophrenia (3), often involving musical or semantic content. Analogies between tinnitus and phantom pain (pain localized to a limb or organ not physically present in the body) are commonly made (13, 76-79). Tinnitus and phantom pain are phantom perceptions whose exact underlying mechanisms are unknown - both are difficult to measure, have heterogeneous origins, are influenced by emotional and environmental factors and often prove problematic to treat (78).

The most common type of tinnitus classification is according to whether it is subjective or objective (3, 73, 80, 81). Objective tinnitus is perceivable by others in addition to the tinnitus sufferer - it is a tangible mechanical sound which is generated internally within the body (for detailed discussions, see (80)). However, objective tinnitus, sometimes classified as somatosound, is a rare occurrence which only constitutes about 1% of tinnitus cases (3, 73). Subjective tinnitus is perceived solely by the tinnitus sufferer (3, 73, 80) and is considered to represent an auditory phantom phenomenon (2, 7, 82). Whilst it is acknowledged that objective tinnitus can occur, the word tinnitus hereafter refers to subjective tinnitus which is the focus of this thesis. Moreover, due to its impact on the sufferer, the unified percept of tinnitus is usually not just related to the phantom sound itself but also to the affective components linked with the sound percept as well (4, 13, 53, 83).

2.1.2 Demographics

There is a high prevalence of tinnitus worldwide - estimates from studies range widely from 4-32% (12, 15, 84, 85). This disparity is believed to be caused by differences in
epidemiological study design and specific questions asked, as well as the heterogeneous nature of tinnitus itself. Prevalence increases significantly with hearing loss (3, 15). Approximately 10-15% of the general population experience ongoing tinnitus requiring medical attention (3, 12, 84-87).

Tinnitus occurrence and distress also increases with age (12, 80, 84, 88, 89). In a study by Hoffman & Reed (12), the highest incidence rate for tinnitus was 8-20% seen in the 60’s and 70’s age group, with subsequent decline in the older age groups. This effect is present independent of influence from noise exposure (84) – it can possibly be attributable to increased occurrence of presbyacusis (89), as well as decreased and/or less effective neuroplastic processes (88). Interestingly, up to one-third of all children can also experience tinnitus, either present at birth (congenital) or acquired during childhood (80, 84, 90, 91). Yet, only 6.5% spontaneously report this (91). Tinnitus rates during childhood are increasing over the years, hypothesized to be due to the increased occurrences of otitis media (84).

Males experience tinnitus more frequently than females, nonetheless, they are less likely to report it or report being distressed by it than women (34, 74, 80, 92-94). Moreover, men generally have higher (worse) hearing thresholds than women, a finding partly attributable to greater lifetime occupational noise exposure (84). They also do not use as much noise protection as women (94). In general, men appear to report somatic symptoms less and display less noise annoyance than women (94).

Increased tinnitus may also be associated with lower socio-economic status in some countries (34). Tinnitus sufferers were less likely to be in employment, but it is not known whether this is a consequence of the tinnitus distress or a pre-existing factor (93). The influences of age, gender and SES on tinnitus are not autonomous and can interact with each other (34, 86). These interactions are still under study.

2.1.3 Causes, Risk Factors and Co-morbidity

It is important to note that tinnitus is not a disease in itself, but is a presenting symptom in various underlying diseases and pathologies (29, 73, 75, 80). If a cause is discernible, it is most likely to be otology-related and in particular NIHL (34, 75). Other reasons include neurological pathologies, various infections and administration of certain pharmaceutical drugs (2, 34, 35, 95, 96) (see Table 1 for a list of possible causes). In 50% of cases, however, the cause remains unknown (80). One possibility is that other factors (e.g. psychological,
physiological stress, etc.) may drive tinnitus perception in these cases. Some sufferers can modulate tinnitus loudness and annoyance by altering various dietary and lifestyle factors such as: hydration, alcohol and caffeine, sodium intake, monosodium glutamate (MSG), stress and sleep patterns (3, 85, 97). These interactions are highly variable, multifaceted and dependent on the individual itself. Presbyacusis and NIHL serve as tinnitus risk factors due to their high rates of co-existence. Vernon & Meikle (29) reported that 70-80% of tinnitus patients sampled had significant hearing losses. However, it is possible for individuals with normal hearing thresholds to also experience debilitating tinnitus (80). Tinnitus and chronic pain are also commonly found together; especially temporomandibular joint disorder (TMJD), which can be present in up to 60% of tinnitus sufferers (75). Hyperacusis, which is an abnormal oversensitivity or intolerance to sounds, can develop in about 40% of tinnitus patients (34, 75).

2.1.4 Tinnitus presentation

The presentation of tinnitus in multiple forms may be partly related to the fact that it can have various underlying causes (58). Ringing in the ear is a common lay reference to tinnitus, however, it has also been described by some sufferers as whistling, hissing, buzzing, roaring, pulsing or sizzling (34, 75, 81, 98). Tinnitus can be perceivable in just one ear (unilateral) or both ears (bilateral), as coming from the centre of the head (central), and rarely, as outside of the head. Unilateral tinnitus is more commonly reported (84, 98), but whether there is a left or right ear dominance is debatable (84). Tinnitus can be of any pitch but is often matched to be above 3000 Hz (75, 81). Although the audiogram is only a gross measure of deafferentation, it does appear to have a relationship to the perceived tinnitus sound. Tinnitus tends to localize toward the ear with greater hearing loss (99). Tinnitus pitch matches tend to be higher pitched for high frequency hearing loss and lower for hearing loss that extends into lower frequencies (99). Tinnitus likeness matching processes have suggested that tinnitus can be reasonably well replicated as a spectrum that mirrors the audiogram (6, 19). Further variability is added in that it is possible to hear one or more type of tinnitus sound, consisting of simple or complex sounds, of constant or varying loudness and that is either continuous or
Table 1. Possible causes of subjective and objective tinnitus (adapted from (25), p. 905).

<table>
<thead>
<tr>
<th>CATEGORIES</th>
<th>CAUSES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Subjective</strong></td>
<td></td>
</tr>
<tr>
<td>Otologic</td>
<td>Noise-induced hearing loss, otosclerosis, otitis, impacted cerumen, sudden deafness, Meniere’s disease and other causes of hearing loss.</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Head injury, whiplash, multiple sclerosis, vestibular schwannoma or other cerebellar-pontine-angle tumours.</td>
</tr>
<tr>
<td>Infectious</td>
<td>Otitis media and sequelae of Lyme disease, meningitis, syphilis and other infectious or inflammatory processes that affect hearing.</td>
</tr>
<tr>
<td>Drug-related</td>
<td>Common side effect of many drugs such as salicylates, non-steroidal anti-inflammatory drugs, aminoglycoside antibiotics, loop diuretics and chemotherapy agents.</td>
</tr>
<tr>
<td>Other</td>
<td>Temporomandibular joint dysfunction and other dental disorders.</td>
</tr>
<tr>
<td><strong>Objective</strong></td>
<td></td>
</tr>
<tr>
<td>Pulsatile</td>
<td>Carotid stenosis, arteriovenous malformations, vascular tumours, valvular heart disease, states of high cardiac output and other conditions causing turbulent blood flow.</td>
</tr>
<tr>
<td>Muscular or anatomical</td>
<td>Palatal myoclonus, spasm of stapedius or tensor tympani muscle, patulous Eustachian tube.</td>
</tr>
<tr>
<td>Spontaneous</td>
<td>Spontaneous otoacoustic emissions.</td>
</tr>
</tbody>
</table>
intermittent. Different brain regions appear to be activated for the various tinnitus perceptual types (100).

The length of time tinnitus lasts for is important clinically. Transient tinnitus (which was not previously present) was experienced by 94% of people when placed in extremely quiet conditions, such as an anechoic chamber or room (101). Such occasional tinnitus is very rarely a problem for the person experiencing it. Acute tinnitus is usually transient and retractable, lasting for a few hours to a few weeks, but can bring a person to consult a medical practitioner (3, 73, 75, 102). Causes for acute tinnitus include middle ear infections (otitis media), ear wax, head or neck injuries, certain vascular problems or certain medications. Chronic tinnitus is generally defined as that which lasts for greater than six months (3, 72, 75). Unfortunately, in a certain proportion of the population, tinnitus is an ongoing phenomenon which can last throughout the lifespan. There is insufficient evidence to conclude whether the brain networks remain unchanged between acute and chronic tinnitus, or whether there are changes in the regions involved or strength of connectivity (4).

2.1.5 Effects of severe chronic tinnitus on the sufferer

Chronic tinnitus seriously reduces the quality of life in about 15-20% of those who perceive it (14, 73, 95). Common manifestations of severe tinnitus include impaired concentration, problems with hearing, irritation and annoyance, anxiety, depression, disruption of everyday activities and disturbed sleep (13, 84, 87, 93, 103). These negative effects are reported to be similar to that seen with other chronic health problems (13). Sleep disturbance is prominent and reported in half of severe tinnitus cases (16, 104) and can also act as a precursor for the other observed effects (13). In very rare cases it is thought that chronic tinnitus may contribute to suicide (13). It is uncommon for children with tinnitus to report distress or be affected by it - those who do so report very similar problems to adults, and can exhibit additional problems at school (105). It is uncertain why some individuals are more affected by tinnitus than others. The psychoacoustic characteristics of the tinnitus itself (quality, pitch, loudness) or the individual’s hearing thresholds are not related to perceived severity (16, 86, 106). Several studies have attempted to pinpoint the brain networks exclusively involved in tinnitus distress (4, 9, 83, 107, 108). Gender differences are present with regards to the emotional reaction to tinnitus, with men and women with identical tinnitus type, intensity and
distress experiencing differences in mood, correlating with different regions of brain activation (58).

2.1.6 Tinnitus Assessment

A useful clinical framework developed by Searchfield & Jerram (109) for assessment, which is in line with current clinical practice, involves measuring tinnitus within a three dimensional matrix – along the three axes of psychology, physiology and psychoacoustics. A full assessment battery is carried out including history taking and questionnaire administration, audiometric testing, and tinnitus psychoacoustic characteristic matching. Tinnitus assessment needs to be consistent in order for treatment outcomes to be validly compared, and be used by all cultures in a similar manner (102).

Tinnitus history questionnaires (110-112) are commonly administered to examine tinnitus onset and characteristics, general health and medical history, and noise exposure history. Complementary to this, tinnitus impact questionnaires provide indications about quality of life effects as a quantitative score. These are generally reliable and valid measures (3, 18, 110, 112). Identifying the status of an individual’s hearing is also imperative given the high association between hearing loss and tinnitus (75, 80). A full audiometric test battery is conducted comprising of pure tone audiometry (including high frequencies for tinnitus assessments), speech audiometry, Immittance and Otoacoustic emissions (OAE) measures (105).

Psychoacoustic tinnitus matches comprise of pitch and loudness level match (LLM), minimum masking level (MML) matching and residual inhibition (18, 20, 98, 113). These tests are well-established and have been in clinical use for at least the past 30 years (20, 113). Psychoacoustic measures serve a useful role for monitoring treatment effect on tinnitus perception, especially LLMs and MMLs (18). Pitch matching (in Hz) identifies which frequency of external sound is judged by the individual to be most identical to that of their tinnitus. A pitch match is obtainable in the majority of tinnitus sufferers (20, 113). With LLM (in dB SL), the level of noise (played at the tinnitus pitch) which is most identical to the loudness of tinnitus is determined. Tinnitus sufferers often report subjective tinnitus loudness (measured using visual analogue scales, etc.) to be very high, although objective loudness matches are to relatively low levels – this has been termed the tinnitus loudness paradox (20, 37). One reason for the low level match of tinnitus may be recruitment; however recruitment
cannot fully explain the gap between reported loudness and matched loudness (114). The use of sensation level has been criticised with the suggestion that conversion to phons (unit of loudness level for pure tones) (115) occur. However, despite these criticisms SL is the defacto standard because of its ease of use, and the failure of other scales to eliminate the loudness paradox. MML (in dB SL) is the minimum level of masking noise needed in order to just cover up the perception of tinnitus (20, 109). Residual inhibition is the temporary suppression of tinnitus (reduction in volume) following presentation of external sound (113). Clinically, this is often assessed by applying MML noise at 10 dB SL (10 dB above hearing threshold) for 30 seconds. This inhibition usually lasts seconds to minutes, and can serve as a rough indication of whether 1) the tinnitus match is appropriate and 2) the individual will respond to sound therapy or not (113). Tinnitus location or “where” has not been considered much when evaluating tinnitus clinically, although studies have been conducted with 3D location matching (116). 3D sounds can be accurately used to assess perceived tinnitus location of tinnitus sufferers and has been indicated to be more beneficial than conventional masking in terms of preference and reduction in tinnitus impact scores (116).

When collated together, these measures enable an individual to be placed accurately within the three-dimensional assessment matrix (109). Consequently, interventions can be tailored to meet specific patient needs. For example, one may score high on the psychological axis, but have no hearing loss therefore is low on the physiological axis, and have low levels of psychoacoustic matches. In this case, management would be more psychological-based, involving counselling, relaxation techniques, attention training, etc.
2.2. Tinnitus mechanisms and models

2.2.1. Genetic basis

Due to the lack of studies, it is still debatable whether there is a genetic basis for tinnitus (2, 3, 35, 59). Molecular/genetic factors for tinnitus susceptibility (if present) are currently unknown. A variant in the serotonin transporter gene (5-HTTLPR) which is associated with depression has been studied, but no association was found (117). Goto et al. (118) observed that brain-derived neurotrophic factor (BDNF) gene expression levels correlated with tinnitus severity. Patients with mild tinnitus had significantly greater levels of BDNF than severe tinnitus or control groups. BDNF is found throughout the central and peripheral nervous system and plays an important role in development of the auditory system (involved in creating neurons, cell differentiation and cell survival) (119, 120). Following acoustic trauma, BDNF gene patterns of expression have been observed to change and increase in the spiral ganglion neurons and IC, and further on in time, decrease in the primary auditory cortex (121). This is a budding area of research however and it is still in its early stages.

2.2.2. Physiological observations and models

The precise mechanisms giving rise to tinnitus are still not completely understood and no single theory of mechanism is universally accepted (35, 67, 102, 107, 122). Physiological focus on tinnitus has largely been around the cellular basis of tinnitus generation, and development in this field has been vastly aided by advances in neuroimaging techniques (59, 107).

The main premises of current physiological models are:

1. Tinnitus is generated as a result of peripheral deafferentation or top-down noise-cancelling deficits
2. Central compensatory processes take place to adjust for altered auditory input, giving rise to the sensation of tinnitus
3. Multiple overlapping networks in the cortex are involved in tinnitus perception, including emotion, memory and prediction, arousal, attention, and which reflect the affective component or distress associated with it
A conceptualization of these premises is provided in Figure 1.

Figure 1. The main premises of tinnitus physiological models (boxes) with key theories/models in italic text under each relevant premise. The arrows indicate possible associations between the different factors proposed to give rise to tinnitus perception.

Not all patients with peripheral lesions experience tinnitus, however, and it is now generally recognized that tinnitus sensation and tinnitus perception are not identical (4, 78). Sensation can be defined as the effect of a stimulus on sensory receptors (123). The organization of this stimulus within an individual’s schema and its meaningful interpretation gives rise to perception (78). Auditory cortex activation evoked by an acoustic stimulus does not necessarily produce conscious auditory perception (4). Likewise, in the case of tinnitus, a stimulus is not necessary for perception (124). Perception of tinnitus may involve networks corresponding to conscious awareness (4).
2.2.2.1. Tinnitus Generation

Peripheral deafferentation

Tinnitus was initially believed to be generated in the peripheral auditory system (either the inner ear or the auditory nerve) (81), due to the high co-occurrence of hearing loss and common complaints of difficulties with hearing among tinnitus sufferers (12). However, this proposition is not supported by empirical research (2, 34, 78, 82). Tinnitus generally persisted following transection of the auditory or vestibulocochlear nerve; in certain cases, it is made worse (34). Peripheral lesions or deafferentation may be a common trigger, but by itself may not be a sufficient condition to develop chronic tinnitus (96, 125, 126). Instead, current animal models and neuroimaging evidence suggests that tinnitus is essentially a central phenomenon, generated within the central nervous system with cortical and sub-cortical involvement (2, 34, 59, 76, 78, 127, 128) as a result of altered auditory input (2, 3, 34, 129, 130). It is possible for non-peripheral factors (such as central auditory pathway injury, or transection to brainstem structures) to also elicit tinnitus in some cases (3, 34). These changes cannot always be picked up using standard audiometry. Alterations to various biochemical pathways within the auditory system have also been researched regarding their potential role in tinnitus generation (for detailed discussions, see (131)). The heterogeneous nature of tinnitus is such that it can potentially be generated by various mechanisms (34, 86). Moreover, more than one mechanism may be responsible for tinnitus generation in an individual (3, 34).

Gating models

Some researchers suggest that alterations to incoming input are not sufficient to generate central tinnitus signals: alterations to top-down inhibitory mechanisms are also necessary (8). A limbic-auditory gating mechanism has been described by Rauschecker et al. (8), whereby components of the limbic system (the nucleus accumbens and ventral medial prefrontal cortex) normally act as a noise-cancellation mechanism at the level of the thalamus and prevents the tinnitus signal (unpleasant, unwanted noise) from reaching the level of conscious perception in the cortex. If the limbic system becomes compromised, e.g. change in emotion, it is possible for the tinnitus neural signals to be relayed to higher centres and be perceived. A key drawback of this gating model is that it is not congruent with current neurophysiological models of emotion, which suggest that emotional auditory stimuli are already initially
processed and decoded in the auditory cortex before being relayed to the amygdala for emotional interpretation (132, 133).

2.2.2.2. Central compensatory processes

The primary aim of homeostatic neuroplasticity is to minimize disruption and maintain a mean (or optimal) level of neural activity within the auditory system (134). This is done by compensating for changes in input, which are most likely to occur by learning or alterations to typical sensory input. The theories and models discussed below essentially argue for a specific form of homeostatic process as generating tinnitus perception. As of now, there is no one physiological model which explains the tinnitus signal (35, 67, 102, 107, 122). It is also not known whether the changes observed are specific to tinnitus or if they reflect the commonly co-existing condition of hyperacusis instead (67).

Gain models

Gain broadly refers to an increase in the volume or signal output of a neuron; a change in the steepness of the curve in an input-output sound function of a neuron (135). An integrative framework of abnormal central gain suggested by Norena (136) describes tinnitus arising as a result of increase in neuronal sensitivity or gain in order to adapt to reduced sensory input, while preserving mean firing rate and coding efficiency. As a result, so-called “neural noise” is also amplified and perceived as tinnitus. Spontaneous neuronal hyperactivity (pathologically increased firing rates of neurons) has been observed at various levels of the auditory system, including the DCN, the IC and the AC (14, 68-70). These changes have been recorded following noise exposure as well as ototoxic drug administration (14). Ascending pathway gain models may more readily explain hyperacusis, which is associated with enhanced sound-evoked activity in multiple-auditory processing centres (IC, MGB, AC) in contrast to tinnitus, which may arise solely by increased central gain in the AC (137, 138).

Cortical reorganization and homeostatic plasticity

Cortical reorganization tinnitus theories propose that due to the tonotopic arrangement of the auditory cortex, neuronal networks for frequencies adjacent to that of the hearing loss (the “edge frequencies”) expand and take over cortical areas receiving reduced input (96, 113). Over-representation of neuronal response corresponding to the edge frequencies will subsequently result in tinnitus with similar pitch, as commonly observed clinically (3, 34,
Cortical reorganization evolves on a slow time scale within several days or weeks (96). This process may be driven by structural plasticity; axonal and dendritic connections are formed and strengthened for regions corresponding to the edge frequencies, while other connections are disrupted or weakened (95, 96). Norena & Eggermont (27) mention based on animal study findings that the prevention and reversal of cortical reorganization can potentially alleviate tinnitus symptoms. However, human neuroimaging studies have observed no differences in tonotopic arrangements between individuals with tinnitus and healthy controls (139, 140). Therefore, whether tonotopic map changes play a causal role in tinnitus generation is still a matter of debate.

Another form of homeostatic plasticity which works by reducing inhibitory synapses has also been hypothesized to be activated (141). Weakened inhibitory synapse and strengthened excitatory synapses have been observed in the auditory cortex following cochlear ablation (142), resulting in enhanced neural excitability, potentially also leading to elevated spontaneous cortical activity and tinnitus perception (143). An animal study by Yang et al. (141) showed that high-frequency hearing loss resulted in two different cortical changes within the primary auditory cortex. There was a region with sensory deprivation, which demonstrated decreased inhibitory synaptic transmission. In the second region, which fell under normal hearing, there was both inhibitory and excitatory transmission and cortical map reorganization. The animals demonstrated tinnitus with tinnitus pitch falling in the region of sensory depression. Moreover, drugs which were administered in the study to enhance inhibition of neural transmission eliminated tinnitus, while those which reduced neural excitation did not.

**Abnormal neural synchrony**

Rhythmic or repetitive neural activities are present within the cortex, termed neural oscillations (144). These are labelled according to bands of frequency oscillations as follows: delta (approximately 1.5–6Hz), theta (approximately 6.5–8Hz), alpha (approximately 8.5–12Hz), beta (12.5-30Hz) and gamma (approximately 30–60Hz) (100, 144-146). A high-gamma band may also be measured typically between 50-200 Hz (147). Various brain functions are realized by simultaneous oscillations or coupling between different bands (148). According to the Thalamocortical Dysrhythmia theory (TCD) (149), reduced incoming signals/increased inhibition of signals arriving at the thalamus triggers an adaptive cascade of
events. There is a decrease in information which needs to be propagated to the next sensory level. Spontaneous resting state alpha rhythms exhibited in thalamocortical loops subsequently move to theta band rhythms (67, 149-151). This has been described as if the thalamocortical columns in the affected regions are “asleep” (150). Due to GABA-mediated lateral disinhibition processes, particularly in temporal regions relating to edge frequencies, gamma band activity also increases (67, 145, 146, 150). In cases where the deafferentation spans across numerous pitches, missing information is retrieved from auditory memory (parahippocampal region) via theta-band firing. Increased theta-gamma coupling will also ensue whereby theta waves act as carrier waves by which burst-firing allows for recruiting and synchronizing different long-distance neural networks simultaneously: this may form the neural basis of consciousness for tinnitus (67). TCD has also been applied in the past for various neurological disorders such as Parkinson's disease, chronic pain, epilepsy as well as depression (149).

**Other theories**

Schlee et al.(152) propose a global workspace theory in which tinnitus arises due to hyperactivity that spans across the cortex, leading to increased global activity. Sensory stimuli have the ability to activate excitatory neurons spread across the cortex via long-range cortico-cortical axons, which can form a global workspace for carrying out various cognitive processing (153). Moreover, sensory stimuli may compete with each other; such that any global activity activation inhibits other stimuli from being consciously processed. Multiple and parallel cognitive processing modules may be recruited to the processing of the tinnitus neural signal by top-down attentional processes; this ultimately results in conscious perception of tinnitus (4, 67, 152). Connections between the auditory cortex and frontal regions may form a part of consciousness tinnitus networks, as neuromodulation techniques administered to the frontal cortex were also reported to modulate tinnitus loudness (154).

A new proposition is that dysfunctional prediction processing may drive tinnitus perception (7, 67). The Bayesian brain hypothesis states that in situations of uncertainty, the brain relies on internal probabilistic models to optimize function (155). Incoming sensory input is combined with existing prior knowledge to generate predictions. At each level of the sensory processing hierarchy, the difference between incoming sensory input and existing internal memory representation, the prediction error only, is passed onto the next level for processing.
According to De Ridder et al. (7, 67), deafferentation at the peripheral auditory level results in missing input reaching the cortex for certain frequencies which generates a topographically-restricted prediction error. Subsequent central plasticity processes focus on and attempt to compensate for this error, ultimately giving rise to the sensation of tinnitus. This is a novel theory with limited empirical studies currently conducted on it.

### 2.2.2.3. Tinnitus cortical networks

There is now general support from most physiological models that final tinnitus perception and/or distress arises as a result of integration between various auditory and non-auditory networks, including emotion, memory, arousal and attention. Tinnitus network models attempt to define which specific cortical structures may show altered neuronal activity and altered connectivity in tinnitus (59, 78, 79, 128, 156-158). Current network models of tinnitus are largely based on functional neuroimaging evidence and show overlap with regions corresponding to attention, emotion and memory networks (Figure 2) (4, 59, 78, 128, 159). Differences in activation patterns in these regions are also present between individuals with distressing and non-distressing tinnitus (78, 79). These higher-level influences potentially explain the lack of correlation between tinnitus psychoacoustic characteristics alone and tinnitus severity. There is some ambiguity regarding whether the auditory cortex is part of this distress network. Schecklmann et al. (160) observed the level of tinnitus distress to correlate negatively with the volume of grey matter in the bilateral auditory regions; this may indicate interactions between tinnitus perception and distress in the auditory regions. These networks are different depending on the underlying pathophysiology giving rise to tinnitus, and can also shape psychological responses to the tinnitus (4). Moreover, these resting-state tinnitus neural networks have been observed to change as tinnitus duration increases, becoming stronger, eliciting stronger synchronization and becoming more robust to change (79, 88). Essentially for network models, large-scale integration is needed to bind together various anatomical and functional regions of brain activity to form a unified tinnitus percept and cognition. Although the mechanisms involved are not clearly understood, oscillatory frequency-coupling processes previously discussed may form the fundamental pathway for recruiting different modules across the cortex (67).
Figure 2. Example of a tinnitus brain network model for tinnitus perception and distress. Alongside the auditory cortex, regions of subgenual (sgACC), dorsal anterior cingulate cortex (dACC), posterior cingulate cortex (PCC), precuneus, parietal cortex, hippocampus, frontal cortex, amygdala and anterior insula have also been identified. These regions overlap with memory, emotion, and attention networks. Reproduced with permission from (78), p.8077.

Tinnitus loudness and pitch can change in approximately 2/3 of tinnitus sufferers by various somatic manoeuvres such as altering eye gaze, jaw movement, applying pressure to the head (tensing neck muscles), or touching the hand (1, 161). Moller (1) has outlined how the non-classical auditory pathway may establish this link. Within this pathway, there are neural connections at the level of the DCN and IC between auditory and somatosensory systems, such that the firing rates and timing responses of auditory information being transmitted to the cortex is also dependent on parallel incoming somatosensory signals, and vice versa - termed crossmodal interactions (162). Moreover, tinnitus representations can be connected to muscular responses at various levels of the central nervous system; these responses can be increased by emotions such as fear and anxiety (128). This is in line with observations of tinnitus sufferers frequently experiencing increased muscle tension in the neck and lower face, that is also associated with aversive tinnitus responses (128).
Psychoacoustics is the broad term given to study of the perception of sound, focusing on the physical (e.g. vibrations of air particles), physiological (e.g. construction of the ear), and perceptual (e.g. auditory sensations) correlates of sound production, transmission, and reception (69, 163-165). Specific psychoacoustic models of tinnitus are scant in the literature compared to physiological models. Welch & Dawes (74) have applied the Theory of Signal Detection model (166) to tinnitus perception and to explain individual differences in tinnitus awareness. The signal detection model states that there are several factors which determine the ability to discriminate between a stimulus and random or background activity (noise). The threshold of detection, called the criterion placement, can change based on awareness, experience, physiological state, adaptation or purpose/goals. Sensory gain adaptation within the auditory system (response to peripheral deafferentation) may result in shifts of the detection criterion placement, making it more likely that any given level of internal neural noise signal is consciously detected by the brain and perceived as a tinnitus signal (167). Individuals with increased awareness can also have the criterion placement towards a lower signal detection threshold, whereas others require stronger signals to be present before reporting tinnitus. As a result, further cortical processing and ultimate awareness of the tinnitus is increased. The Adaptation Level Theory Model (ALT) of tinnitus perception (5) is a unique psychoacoustic model which integrates several findings regarding tinnitus-external sound interactions into one coherent framework. It is discussed separately in Section 2.5. Adaptation Level Theory and Tinnitus.

Studies which have been conducted in this field have mostly focused on individual properties of tinnitus. Penner et al. (36-39) concluded that tinnitus is an unstable signal based on variability in tinnitus loudness and pitch matches over multiple measurements. A common perceptual observation is the tinnitus loudness paradox: a discrepancy between the subjective magnitude estimation of tinnitus (often reported as a loud sound), while objective loudness level matches remain at a low level (usually below 20 dB sensation level) (37). This effect is only partially explainable by loudness recruitment (114), which is a rapid growth of loudness perception often observable among individuals with hearing loss due to reduced dynamic range of hearing. Henry & Meikle (114) observed approximately 25% of the variability in loudness level matches was explainable by loudness recruitment.
Psychoacoustic studies of tinnitus masking, or the covering of tinnitus by an external sound, have also been conducted. Tinnitus does not follow the normal energetic masking patterns as external sounds, whereby interference is physiological and at the level of the cochlea when the masker sound overrides that of the original signal (168). There is no specific relationship between tinnitus frequency spectrum and effectiveness of masking; tinnitus with a broadband sound spectrum (consisting of several pitches and which would typically span across several sites on the cochlea if it were an external sound) can be covered by a masker of a single tone or pitch (42). Moreover, unilateral tinnitus in some individuals can be effectively masked by tones presented to the opposite ear to that where tinnitus is perceived (42, 169). Unilateral masking may also provide successful relief from bilateral tinnitus (29, 113, 170). This reflects interactions between the tinnitus and masking stimuli higher up along the auditory pathway where binaural integration occurs (171). Moreover, over time the level of masker may have to be raised considerably in cases to continue covering the perception of tinnitus – Penner et al. (172) observed an increase of sound level over 45 dB was needed to continue masking tinnitus over a duration of 30 minutes.

It is possible that tinnitus undergoes a different type of masking, called informational masking (38, 39, 171, 173-175). This term describes the elevation of auditory thresholds in the presence of masking stimuli which cannot be accounted for by energetic masking alone (168). It is thought to involve central auditory processes, possibly due to competition for cognitive resources for neural processing between the tinnitus signal and masking signal (171, 175, 176) (171). Representation of the neural tinnitus signal itself is unaffected. Informational or “central” masking is possible with tinnitus as the phenomenon is due to central processing itself. While the precise mechanisms of such masking is not completely understood, as mentioned above, competing for the brain’s cognitive resources may be a key factor (158). Specific categories of tinnitus masking patterns have been proposed by Feldman (42) that vary depending on the intensity of sound needed to mask the tinnitus. If a low sensation level of sound can mask tinnitus across the frequency range it is termed congruence; if a high sensation level sound is required it is called distance. In cases, the tinnitus may not be masked at any sound intensity and this is defined as persistence. According to this view of central masking, tinnitus may be better masked by maskers with dynamic properties in terms of loudness, timing, and pitch changes over time, which can provide greater cognitive interference (177).
2.2.3. Psychological observations and models

Psychological processes related to changes in thinking and behaviour can intimately tie in with underlying neurophysiological tinnitus changes, and form the connection between tinnitus perception and resulting emotional affective response to it (20, 59, 178-181). Hallam’s habituation model (181) suggests that the majority of people with tinnitus undergo natural adaptation over time, or habituation. In a small minority, habituation may be prevented because of an inability to shift attention away from the tinnitus, due to the signal’s increased salience (181-183). General excessive attentiveness towards sounds and an inability to habituate to external sounds has also been observed among tinnitus sufferers (182). In an electrophysiological study, tinnitus complainers showed less diminution of measured neural responses over time to a series of administered tone pips than tinnitus non-complainers, reflecting general difficulties in sound habituation (184).

Sweetow (178, 179) states that maladaptive (catastrophic and dysfunctional) thoughts regarding tinnitus can drive tinnitus distress by increasing perceived tinnitus severity and emotional distress. Lack of control and intrusiveness felt by the individual as a result of the tinnitus may be more debilitating rather than individual tinnitus characteristics (pitch, loudness, etc.). Budd & Pugh (180) highlighted relevant aspects of maladaptive thinking about tinnitus, such as wishful thinking that the tinnitus will disappear or reminiscing often on how it arose. Understanding that the tinnitus will not disappear and learning to view the tinnitus as a neutral factor in the individual’s everyday life is proposed to lower tinnitus severity.

Jastreboff’s neurophysiological model of tinnitus (59, 183, 185) states that when an individual displays negative emotional reactions in response to tinnitus (such as anxiety, fear, frustration, anger) or becomes stressed by it, the limbic and autonomic systems are activated simultaneously with the tinnitus signal (23, 40, 118). If this occurs frequently, classical conditioning results in the reinforcement of negative emotional responses each time tinnitus is perceived, until it becomes an automatic response.
2.3. Tinnitus Treatment and Interventions

Tinnitus cannot currently be ‘cured’, however a variety of options do exist for managing the condition (20, 22, 75, 186, 187). Interventions can be either aimed at reducing the perception of tinnitus, reducing distress caused by tinnitus, or a combination of both (35, 188). Sound therapy is of most relevance to this thesis and is focused on in this section. While an in-depth review of all other potential tinnitus treatments (in development and currently implicated) is outside the scope of this document, the most prevalent treatment paradigms are also briefly outlined below. The heterogeneity of tinnitus can make it a complex and difficult condition to manage. The most successful management programs have used a combination of treatments which are customized for the needs of each individual (20, 189).

A recent systematic review of current tinnitus treatments by Langguth et al. (35) concluded that applying current tinnitus treatments to tinnitus sufferers is significantly more beneficial than leaving them untreated. A comprehensive diagnostic assessment is essential to identify the etiology and other coexisting conditions in an individual and this can enable for applying an individualized treatment plan. Increasing evidence suggests that there are different subgroups of tinnitus which differ in their pathophysiology, presentation, modulating factors and treatment responsiveness, e.g. tinnitus arising as a result of temporomandibular disorder is typically different from that arising from noise trauma (6, 35, 102, 189). However, it remains difficult to differentiate tinnitus into different subgroups (35, 102). The existence of subgroups may explain why many treatments fail during clinical trials (47), therefore it is essential to obtain information along multiple dimensions in order to identify clusters in the sample population. Multidisciplinary management is likely to be more successful, taking into account hearing impairment, emotional and attentional, musculoskeletal and somatosensory effects (5, 35, 102, 109). A stepwise protocol or algorithm for diagnosing and managing tinnitus currently exists (35, 102) and is illustrated in Figure 3. Comprehensive understanding of the mechanisms underlying tinnitus will lead to better treatment outcomes for the tinnitus population.
Figure 3. A broad algorithm which might be used for the diagnosis and management of tinnitus patients, adapted from (130).

### 2.3.1. Sound Therapy Overview

A common observation is that tinnitus perception is often affected by the level of sound in the environment (28, 29, 190, 191). This effect lasts longer than of residual inhibition (192), whereby continuous presentation of an external sound results in transient (for a few seconds, sometimes minutes or hours) decrease or extermination of tinnitus. Sound therapy was subsequently developed and is one of the most prevalent tinnitus intervention paradigms today (35). Sound therapy is the use of sound in a manner that provides some benefit to the tinnitus sufferer. It does not identify a particular sound or type of sound; rather it is a number
of different methods, each with its own potential mechanism or overall goal. That is, sound therapy is an overarching term, much like “relaxation therapy” or “cognitive therapy” that can be applied in a number of ways. Some interventions aim to provide immediate relief; others aim for long-term changes in underlying neurophysiological processes. Current intervention parameters can differ on various aspects, such as:

- Presentation location - bilateral, ipsilateral or contralateral to the side of the tinnitus (193)
- Length of wear – hours per day as well as length of total intervention time (20),
- Type of device – wearable or non-wearable (20). Portable and wearable sound therapy devices include tinnitus masker devices, hearing aids or a combination masking instrument (hearing aids which play masking sound) (20, 29, 32, 194). Non-wearable devices are table-top noise generators, CD or MP3 players, pillow speakers, etc. (29),
- Type of sound – NBN or BBN (either pitch-matched or unmatched to tinnitus), environmental sounds or music (28-30),
- and/or
- Sound level

2.3.1.1. Mechanisms of Sound Therapy

Despite the popularity of different sound therapies and emerging neurophysiological evidence for sound-induced brain changes (20, 31, 32), the value and mechanisms underpinning the paradigms are not universally agreed upon. Modification of perception (e.g. frequency, intensity) and/or reaction (e.g. relaxation) are implied in the success of sound therapy (5, 20-24). The immediate benefits are proposed to arise via masking, which reduces tinnitus audibility or makes it inaudible (20, 21). As discussed previously in Section 2.2.3., tinnitus masking is different from normal auditory masking. Furthermore, hearing loss or tinnitus pitch does not correlate with the effectiveness of tinnitus masking (195). Therefore, the clinician must often rely heavily on individual preference and trial-and-error in setting the masker characteristics (an exception is TRT which is highly prescription-based) (196).

In the long-term, the introduction of sound stimuli can potentially prevent auditory deprivation and restore missing sensory input to the auditory system – eliciting neuroplastic changes in the auditory cortex such as a decrease in central gain (22, 136, 197). Reversed or
altered tinnitus-related neural activity has been observed in some animal studies following sound therapy (25-27). Norena & Eggermont (27) observed that when cats were exposed to loud sound and then placed immediately in an enriched acoustic environment (ESE) (in the presence of moderate level noise pitch matched to the hearing loss), there was no cortical physiological changes indicative of tinnitus. These changes were present when animals were exposed to loud sound and no ESE. However, a similar application of ESE to humans, consisting of music with frequency spectrum to compensate for individual hearing loss applied to tinnitus sufferers, did not show significant changes to chronic tinnitus (198).

Sound interventions currently include (but are not limited to):
- Hearing aids/amplification of hearing
- Total and partial masking
- Habituation therapies, e.g. tinnitus retraining therapy (TRT)
- Acoustic desensitization, e.g. Neuromonics
- Relaxation approaches, e.g. environmental sounds
- Neurophysiological approaches, e.g. co-ordinated reset therapy

2.3.1.2. Amplification of hearing

The line of argument in using hearing aids for tinnitus management is that amplification of sound, particularly in pitches corresponding to regions of deafferentation, can restore missing auditory input and reduce central generation of the tinnitus signal (199). Vernon & Meikle (29) reported 70-80% of tinnitus patients sampled in their study to have significant hearing losses. Shekhawat (199) conducted a scoping review of the role of hearing aids as a tinnitus intervention; it was concluded that there is merit in using hearing aids for tinnitus relief, however a need remains for stronger methodology and randomised control trials in this field (199). A limitation to using hearing aids is if the hearing loss (and subsequent tinnitus pitch) is in the high frequencies ranges above 6 kHz, there is limited coverage specifications of the aids and limited benefit (200). Cochlear implants convert sound to electrical signals that are perceived as sound for tinnitus sufferers with profound sensorineural hearing loss (201, 202). Reduced long-term tinnitus perception has been observed in some studies for unilateral (201) and bilateral hearing loss (202) after the introduction of cochlear implants.
2.3.1.3. Total and partial masking

Contrast reduction of the tinnitus signal is an important principle of sound therapy (23, 30, 156, 203), which assumes that incoming sensory signals are processed by the brain in terms of contrast (comparing signals with each other) rather than in absolute value. Problematic tinnitus may arise from high contrast between tinnitus signal loudness and background auditory activity. The new therapeutic sound(s) introduced will theoretically decrease tinnitus/background sound contrast. However, Jastreboff (23, 204) suggests that tinnitus contrast reduction may not follow a simple, proportional relationship with external sound levels.

Total masking (presentation of sound at minimum masking level where tinnitus is inaudible) (29, 194, 205, 206) or partial masking (both tinnitus and sound are heard, but tinnitus is less audible) (32, 186, 187, 207, 208) can be used in tinnitus interventions. A drawback with total masking is that the level of sound may often be too intense and/or uncomfortable (20). This may trigger negative reactions in the individual, leading to increases in tinnitus perception instead (59). Issues have also been raised regarding whether total masking prevents tinnitus habituation from occurring (pro-TRT arguments), however, this has been disputed by empirical evidence. Tyler et al. (26) examined the effects of counselling only, counselling plus total masking or counselling plus partial level mixing point masking (masking applied at a level at which tinnitus and sound therapy stimuli are at equal perceived loudness) randomly assigned to tinnitus sufferers for 12 months. Total masking resulted in the greatest average decrease in tinnitus handicap questionnaire scores (36.4%), followed by partial level mixing point (31.6%) and lastly counselling alone (16.7%). Studies have illustrated that partial masking can be just as effective as total masking in reducing tinnitus complaints among sufferers (29, 194). Various types of partial masking have been developed over the years, and are advantageous as a comfortable level can be set (and often varied according to user preference) (20). If the sound level is set based purely on the individual’s choice of comfort, it is termed the desired listening level (32). Another variation is the lowest effective level masking (186), which is the lowest level of masker that provides adequate relief.

A meta-analysis by Hobson et al. (32) of six studies on a total of 533 patients from current literature concluded that there is no overall evidence for the effectiveness of using general masking devices/noise generators alone as a sole intervention (for both partial and total
masking) for tinnitus. The authors stated, however, that the evidence reviewed was not of high quality and very limited – there was a lack of long-term studies, and most studies did not use masking alone, but with some other combination of counselling, etc. Studies into specific partial level mixing point were also not included.

2.3.1.4. Tinnitus Retraining Therapy (TRT)

The Tinnitus Retraining Therapy (TRT) paradigm traditionally combines directive counselling with BBN applied at partial level mixing point (185, 209). Clinical outcome studies have reported tinnitus improvement in over 80% of patients treated with TRT (209-212). These effects have lasted even after five years post-treatment (197). Kim et al. (213) found that TRT using BBN lead to the highest improvement in tinnitus outcomes, followed by mixed noise (combination of both BBN and NBN) and NBN TRT respectively. On the other hand, Tyler et al. (26) reported total masking and partial mixing point to be equally effective within a TRT paradigm. However, again, the lack of properly controlled study designs limits the extent to which such findings can be accurately interpreted. A Cochrane meta-analysis has stated that no conclusions can be drawn regarding the efficacy of TRT due to a lack of proper randomized controlled trials in this area (214). A systematic randomized study by Henry et al. (22) compared masking (at level set by the individual) and BBN TRT and recorded that both masking and TRT showed improvements in outcomes over time, but TRT patients continued to demonstrate greater improvement after six months.

Also, it is possible for the efficacy of TRT to arise from additional contributions of counselling administered. Dineen et al. (215) observed equal outcomes in individuals who underwent informational counselling only compared to those who had counselling and sound therapy (involving low-level white noise) administered. Bauer & Brozoski (197) utilised a control group (general health counselling) and compared treatment outcomes to TRT. Both methods were found to be effective in reducing tinnitus loudness and annoyance to a clinically significant extent. However, TRT showed a larger treatment effect. Furthermore, the benefit obtained with TRT in tinnitus handicap accumulated over the study time of 18 months. Also, in the Tyler et al. (26) study, counselling alone led to the least outcome improvement compared to both sound therapy and counselling.
2.3.1.5. Neuromonics

The Neuromonics Tinnitus Treatment (NTT) utilizes customized music and counselling, in an acoustic desensitization approach for promoting relief and relaxation (216, 217). After six months of intervention, NTT patients reported greater alleviation of tinnitus symptoms and greater user acceptability than those subjected to counselling and BBN, or counselling only (216). The intervention shows strong promise, but there are concerns regarding lack of methodological transparency and potential bias (218), thus the paradigm would benefit from further examination by independent researchers. Newman & Sandridge (219) observed both ear level masking devices and Neuromonics resulted in significant reduction in perceived tinnitus handicap (with more pronounced benefit for those with more severe baseline tinnitus). The study also concluded that Neuromonics treatment is less cost effective than masking devices.

2.3.1.6. Nature and dynamic sounds

Nature sounds also offer considerable dynamic variability. Schreitmüller et al. (220) observed that nature sounds were more accepted by the listener than white noise, even though nature sounds had greater sound dynamics and higher masking thresholds. The related nature of stimuli to everyday environments may be a reason for it being easily tolerated. Ocean or wave sounds have recently been introduced by several hearing aid manufacturers in their tinnitus therapy devices (221, 222). Surf sounds vary in their temporal characteristics, and have been also advocated as being useful for pain relief in various clinical populations (223-225), relaxation of breathing (226) and lowering blood pressure (227) and enhancing sleep quality among critical care unit patients (228).

2.3.1.7. Auditory Perceptual Training

Auditory perceptual training procedures aim to counteract the neuroplastic changes associated with tinnitus by training the auditory system via frequency discrimination training, intensity discrimination training and/or auditory object identification and localization (210). Active training involves the individual making behavioural responses while passive training does not require any responses (is similar to sound therapy). Hoare et al. (229) found nine out of ten studies in their systematic review of auditory perceptual training to have some
significant change in either self-reported or psychoacoustic outcome measures. However, all the studies had only low or moderate levels of evidence for any significant effects observed. At the moment it is not possible to draw conclusions regarding the effectiveness of auditory perceptual training due to a lack of adequate scientific studies in this field (35).

2.3.1.8. Other neurophysiological approaches

It is possible for sound therapy stimuli to be designed in order to target specific underlying neurophysiological processes of tinnitus. An example of this is Coordinated Reset (CR) stimulation which is aimed at reducing tinnitus-related pathological synchronization (230). Desynchronizing acoustic stimuli are presented as short tones, above and below the tinnitus frequency to counteract tonal tinnitus (231). A pilot study by Tass & Popovych (230) showed significant decreases in perceived tinnitus loudness and annoyance. A significant increase in alpha-band activity (with strongest increases in temporal and prefrontal cortices) and reduction in delta and gamma-band activity was also observed. This has also been proposed as a possible novel therapy for tinnitus. However, this approach does not hold for tinnitus which is non-tonal in nature (consisting of more than one pitch). Another type of dynamic stimulation involves administering customized notched music in which the frequency corresponding to the tinnitus is removed (232). This is proposed to reduce tinnitus perception by enhancing lateral inhibition, and small but significant decreases in tinnitus loudness were observed following one year of customized notched music administration when compared to controls (232).

2.3.1.9. Limitations and future directions

In the early stages of development, the choice of sound stimuli has in part been limited by the ability to generate them: BBN and NBN were popular as these could be created. The advancement of technology and availability of digital sound means past results need to be reviewed. Despite the long history of sound therapy there is an absence of concrete support for any one sound type, level, duration of use or paradigm over any other (35). This is not surprising given current trends for large quantitative clinical trials that minimise considering individual effects. Given the heterogeneous nature of tinnitus it is possible that no single combination of sound characteristics is best (6, 102, 233). The presence of an overarching framework under which various sound therapy parameters can be tested and explored, using
both behavioural and objective data, may enable for better computation of an ideal therapeutic sound for any given individual with tinnitus.

### 2.3.2. Psychological Interventions

The aim of psychology-based interventions is to decrease the effect of maladaptive thinking and behaviour such that tinnitus perception and distress may also diminish (20, 35). Counselling in the context of tinnitus treatment broadly refers to the provision of information and advice regarding the phenomenon. This can occur at various stages of the tinnitus treatment process. Counselling can be effective in rectifying misunderstandings regarding tinnitus, teaching coping strategies and ultimately enabling individuals to accept their tinnitus.

Cognitive behavioural therapy (CBT) for tinnitus is centred on changing maladaptive thought patterns and attitudes regarding tinnitus (20, 234, 235). It is a broad paradigm that has also been applied for depression, anxiety, chronic pain and insomnia (20). Psycho-education about tinnitus, cognitive restructuring (challenging existing thoughts and beliefs), and positive imagery, exposure to tinnitus, stress management training, and learning various behavioural tactics are all possible avenues for intervention. Relaxation training (217) is used commonly with CBT to reduce muscular tension, increase general well-being and tolerance, and in cases gain control over the tinnitus. The effectiveness of CBT is supported by empirical studies - a significant decrease in tinnitus severity, improvement in quality of life and decreases in depression scores was observed following CBT administration (234, 235). However, the subjective loudness of tinnitus remained unchanged and there is no data for long-term follow-up after the trial. Based on meta-analysis evidence (234, 235), it is clinically recommended that all patients undergo CBT when coming in for tinnitus management. However, not every tinnitus patient will consent or is able to undergo CBT and it may not be relevant in cases where the individual is already applying efficient coping strategies but the tinnitus is still disruptive (35).

Habituation Therapy is based on Hallam’s model (182) and serves as a generic term for any intervention which identifies habituation to tinnitus as its goal. It can hence be any (or a combination) of counselling, CBT, relaxation training, sound therapy, etc. Various attention training, attention-shifting, and diversion therapies can also be incorporated into CBT or
habitation therapy (13, 20, 234). Mindfulness Based Stress Reduction Therapy (MBSRT) (236) is a more recent development which consists of meditation and yoga, with the aim of confronting, accepting and alleviating the negativity associated with tinnitus. There is strong preliminary evidence for its effectiveness in reducing tinnitus distress (237). Roland et al. (2015) observed in their pilot study that participation in 8 weeks of MBSRT (238) resulted in significantly decreased tinnitus symptoms and associated impact on life (measured by the THI and TFI questionnaires). Functional magnetic resonance imaging (fMRI) pre- and post-intervention showed increased connectivity between attention networks following administration of the therapy, indicating changes in attention may be involved in the benefit observed (239).

2.3.3. Brain Stimulation

Brain stimulation approaches aim to focally target the neuronal correlates of tinnitus, in order to eliminate the sensation of tinnitus (240). A novel approach is targeted neural plasticity, which aims to specifically reverse the underlying dysfunctional neural circuits thought to generate the tinnitus signal (240). Non-invasive techniques include transcranial magnetic stimulation, transcranial direct current stimulation and transcutaneous electrical nerve stimulation (TENS) and transcutaneous vagus nerve stimulation (TVNS).

Repetitive transcranial magnetic stimulation (rTMS) uses brief magnetic pulses applied to the scalp via a coil (241) Rhythmic application is thought to alter tinnitus activity. Standard rTMS stimulates 1-2 cm within the scalp surface. At the moment, there are contrasting results when evaluating the effectiveness of rTMS using both high (>1 Hz) and low (<1 Hz) frequency administration (242-244). In cases where benefits have been observed, the effect is small and short-lived and highly dependent on individual factors (242, 244). A new H-coil has been recently developed which can stimulate structures deeper into the cortex, termed deep TMS, and this may be able to stimulate structures previously missed and which may be involved in tinnitus (243). Transcranial direct current stimulation (tDCS) delivers a constant low current to the brain via electrodes (245). Administration of negative stimulation or cathodal tDCS results in decreased neuron excitability due to the decreased spontaneous cell firing. The two most common target sites of stimulation investigated for transiently suppressing tinnitus perception are the left temporoparietal area (LTA) and the dorsolateral prefrontal cortex (DLPFC) (154, 245, 246). The effect has been shown to last from seconds
to hours (245). Also, tDCS can result in transient suppression of tinnitus loudness and annoyance but doesn’t seem to impact on long-term tinnitus affective components (247). The site of tDCS stimulation appears to moderate tinnitus perception differently (245), but further investigation is still needed. Engineer et al. (240) highlight that transcutaneous vagus nerve stimulation (TVNS) may play a significant role in modulating cortical plasticity. Repeatedly pairing tones with brief pulses of TVNS reversed the physiological and behavioural correlates of tinnitus in noise exposed rats (248). The authors suggest that pairing sounds with TVNS may provide a new avenue of treatment for certain subgroups of tinnitus. Preliminary results using humans demonstrate some benefit (249), however, TVNS administered by itself did not have any effect (250).

In addition to these types of brain stimulation, various invasive neuromodulation techniques also exist including auditory cortex stimulation, dorsolateral prefrontal cortex stimulation, subcutaneous occipital nerve stimulation, deep brain stimulation and electrical implants to the primary and secondary auditory cortical regions (251-253). These procedures have been shown to decrease tinnitus intensity transiently or permanently (251, 254). However, the obvious disadvantage of invasive techniques is the discomfort and safety issues associated with it.

Neuromodulation can be a promising treatment; however, more research is needed to better understand how these techniques work and how the brain responds to neuromodulation in the longer term. Given that tinnitus is of different frequency and intensity in different individuals, more sophisticated protocols (local and multiple sites of stimulation), optimized parameters and objective outcome measures are needed to tailor the treatment to any particular person’s neural system (35).
2.4. Electroencephalography (EEG)

Electroencephalography (EEG) is a prevalent, non-invasive technique for assessing electrical activity of the brain, most commonly via ongoing measurements of voltage differences between electrode sites placed on the scalp (255). Event-related potentials (ERPs) are measured EEG brain responses which are time-locked to a specific sensory, cognitive, or motor event (255-258). In instances where an auditory stimulus is used to evoke ERPs, the term auditory evoked potentials or AEPs can also be used (255, 256), although it is acknowledged that it is not just the presentation of the stimulus that elicits the response but also various other underlying processing in the brain (259, 260).

2.4.1. Measurement of EEG and ERPs

2.4.1.1. Electrodes

Depending on where the electrode is placed in relation to the pyramidal cell orientation, it will result in different waveform magnitude and polarity (255, 261, 262). A greater number of electrodes will result in higher spatial resolution. Electrode arrangement is generally using the universal 10-20 system based on its location in the lobe (frontal, central, temporal, parietal or occipital) and its lateral plane location (odd numbers for left hemisphere, z for midline and even numbers for the right hemisphere) (263). Often one or two common reference electrodes will be placed at sites on the scalp not generally considered to be influenced by electrical brain activity (e.g. the mastoid bone behind each ear). Voltage fluctuations in the other electrodes are calculated by subtracting the signal from that of the common reference electrodes, using differential amplifiers (inverts the input of one signal and the other is left non-inverted) (264).

2.4.1.2. Data collection, artifact contamination, pre-processing and analysis

The EEG recordings can also pick up electrical activity that is not of cerebral origin. These are termed artifacts (265) and can be grouped into physiological (e.g. muscular movement, eye movement) and extra-physiological (e.g. poor electrode contact, electrical line noise, environmental noise). Artifacts are detrimental to EEG interpretation as non-cerebral potentials may be mistakenly identified as originating from the brain. Various processes are
present in place for isolating the ERP of experimental interest from ongoing background EEG activity not due to brain electrical activity. Filters can be set such that recordings that fall above or below the selected frequency range are attenuated, e.g. high-frequency muscle movement or low-frequency equipment internal noise (266, 267). Because they tend to occur in the same frequencies as ERPs, some artefacts such as eye movements and eye blinks usually cannot be attenuated by filters. These are removed by setting artefact rejection criteria which rejects all recording exceeding certain amplitudes, e.g. 100 mV (unlikely to be a result of neural activity) (266, 268). Likewise amplifiers may be used to enhance signals within the frequency range of interest (267). Epochs are set which define the time range of the EEG time-locked to the stimulus, e.g. 50 ms before stimulus onset to 500 ms after onset (256, 268). Time-locked signal averaging is important for obtaining ERPs, which are much smaller in magnitude to background noise (262). As the same stimulus is presented over several trials or epochs and averages are taken, the signal-to-noise ratio improves (256). The voltage fluctuations observed within the epoch can be interpreted as reflecting brain processes related to the presentation stimulus.

After the signal has been recorded, EEG analysis software is used to estimate the neural generators of ERPs (dipoles) by examining the scalp potential field distribution (269). These regions of underlying activity are also termed sources, and source localization is the process by which complex signal extraction techniques and algorithms are employed to simulate which dipoles best account for the scalp potentials. A number of pre-determined (or a priori assumptions) and constraints are given at the start to limit the number and location of dipoles to be modelled, e.g. the auditory cortex for auditory ERPs (270). The equivalent current dipole (ECD) is defined as a hypothetical source (269, 271, 272). The final dipoles have six parameters which define them: three spatial coordinates in space (x, y, z), orientation angles (along horizontal and vertical plans) and strength - these can be adjusted such that the fit is optimal (269). The aim is that the final observed field distribution of potential activity should be not be statistically significant from that which would be produced by an ECD. The accuracy of source localization can be affected by head-modelling errors (placement of electrodes, differences in volume conduction within the head, etc.), source-modelling errors (related to the process by which sources are extracted) and general EEG noise (267, 269, 270).
2.4.2. Components of ERP

EEG recordings pick up late latency ERPs which are proposed to reflect the arrival and processing of information at the cortex (271-273). While it is also possible to record auditory brainstem responses (waves I-V, measured at the scalp and reflecting electrical activity in various ascending auditory pathway structures between the cochlea and the cortex) (258), discussion of these are beyond the scope of this thesis. Common auditory late latency waveforms are described below, including the P1, N1, P2 and N2 which can also combine to form a P1-N1-P2-N2 ERP complex (256, 258, 272). Other waveforms include the Mismatch negativity (MMN) and P3 (274). Two ERP waveforms not discussed in detail here, the N4 and P6, can also be readily picked up by EEG, and are related to higher-order (and more abstract) language, semantics and sentence comprehension (N4) and syntactic violations and memory recognition and recall processes (P6) (258, 259, 267, 271). Topographic scalp distributions provide information regarding the electrode sites where maximum waveform amplitudes are typically present, and are useful in instances where various cognitive processing is occurring, leading to simultaneous ERPs at different regions of the cortex. Debate remains over the exact origin and function of these components (257, 267).

2.4.2.1. Common waveforms

P1 (or P100) – The P1 is a positive deflection of the ERP waveform which occurs at a latency of roughly 50-80 ms, and mean 60 ms (256, 258). Greater P1 amplitudes are observed over frontocentral regions of the scalp; however, it has a shorter latency over the posterior regions. This waveform is not always readily identifiable. The P1 is thought of as a neurophysiological indicator of preferential attention to certain sensory inputs and auditory inhibition of anticipated or repetitive stimuli, e.g. reduction in P1 amplitudes for second click in pair of identical clicks (258). Regions of the supratemporal gyrus, Heschl’s gyrus and medial frontal cortex have been indicated as regions of origin (275).

N1 (or N100) – The N1 is usually readily identifiable in recordings. It can be broadly broken down into N1a, N1b and N1c components which occur at 75, 100 and 130 ms approximately after stimulus onset (260). The N1b component is most prominent at the vertex (top of the head); N1a is most prominent at the temporal sites and N1c more widely distributed at the temporal, frontal and lateral-central sites (276), although the exact contributors are not fully
known. The amplitude of the waveform increases with stimulus intensity until approximately 70 dB HL (277). The N1 is hypothesized to reflect selective attention to the processing and discrimination of the physical properties of stimuli (260). It is not sensitive, however, to combinations of auditory stimulus features suggesting it might be related to the temporary memory storage of information (61). According to Winkler et al. (61), the N1 might also reflect regularity formation in ASA – by being sensitive to sound intensity changes that might cue the presence of novel sound sources.

P2 (or P200) – The P2 waveform occurs between 150-200 ms and upto 275 ms, with a mean of 180 ms after stimulus onset (255, 258). The P2 waveform can also be double-peaked in cases. The N1 and P2 reflect similar underlying cognitive processing – selective attention, stimulus feature detection and change, short-term memory storage - and are commonly referred together as the N1/P2 complex (265). P2 amplitude also increases with memory load and stimulus intensity, and continues to do so for levels above 70 dB HL (277). Topographic scalp distributions of P2 are however less localized than N1 (260) and may have multi-site generators in the cortex, localizing predominantly to the vertex, with considerable primary and secondary auditory cortices involvement as well (265, 278). The P2 may have independent generators to N1 as demonstrated by lesion studies where temporal-parietal damage preserved the P2 waveform but not the N1 (278). Top-down feedback has been proposed to contribute to the P2 for some aspects of pre-attentive processing (279), although this phenomenon is not well understood and it is alterable by cortical neuroplasticity changes (278).

N2 (or N200) - The N2 component is less well studied and displays significant variability between individuals (255, 273). It has a latency of approximately 200 ms and is generated predominantly within the central parietal and supratemporal auditory cortex regions (265). More prominent N2 responses have been observed in situations where there is incongruency between expectation and actual input, such as in tasks where the first stimulus is anticipated to provide information about the upcoming second stimulus, however, the second stimulus does not abide this expectation (280). This discrepancy can be in pitch, intensity, tone duration or inter-stimulus interval. It is therefore thought to signify orienting responses and stimulus discrimination processes and is affected by the physical characteristics of the stimuli (259, 280). However, if the individual does not pay attention to the stimuli the N2 is not elicited. This characteristic distinguishes the N2 from the closely associated MMN waveform.
MMN – Typically occurring at a latency of 100-140 ms, the MMN is consistently generated by deviants and violations to expectations – identical to the N2 – but is also present independent of attention (274). This waveform may reflect underlying cognitive processes of updating memory representations based on the latest deviant (255). Scalp distributions for the MMN have been localized to superior temporal gyrus, temporal plane, frontal regions and the vertex (265). The most common way of eliciting the MMN is via the oddball paradigm whereby a deviant stimulus is occasionally present in a stream of repetitive stimuli under a non-attend condition (255, 274). The MMN is significantly influenced by changes to paradigm characteristics (281, 282). The amplitude is increased with greater degree of deviance, smaller number of trials (less habituation to the response), larger inter-stimulus intervals, and when participants do not attend to the stimuli.

P3 (P3b or P300) - The P300 is a robust waveform (283) which has been commonly studied. It is theorised to reflect underlying updating of memory based on incoming information or elaborating stimulus discrimination (284, 285). It is a positive deflection observed at least 300 ms (and as late as 900 ms) after the onset of an incongruent stimulus (258, 283). However, the P3 amplitude is significantly diminished if an individual does not pay attention to the stimulus, if the stimulus has a high probability of occurring, for dual task vs. single task conditions or with greater inter-stimulus interval (265, 283-285) - this distinguishes the P3 from the MMN. The P3 has been heavily studied in populations with attention deficits, e.g. Attention deficit hyperactive disorder. An oddball paradigm can be also used to elicit this waveform. Donchin & Coles (284, 285) suggest that obvious deviants may elicit shorter P3 latencies while complex stimuli which need more time for evaluation are reflected by a longer latency P3. The activity of the P3 is concentrated over the frontal, parietal and medial temporal regions, although a distributed network may be involved with deeper sub-cortical involvement (278, 286). An earlier P3 component can be elicited (before 300ms) by novel stimuli – reflecting the diverting of attention to process this salient event (280). This has been defined as the P3a response and it has a greater frontal region of activation, supported by observations of diminished waveforms in response to frontal cortex lesions (278).

2.4.2.2. Oscillatory Bands
Another form of classifying waveforms is by bands or rhythms, reflecting typical oscillatory (alternating low and high neuronal excitability) patterns of brain activity as a result of thalamocortical connections between pyramidal cells (150). The band corresponds with the frequency range of the EEG signal (67, 287) (Table 2). Some bands can be further broken down into characteristic sub bands. Different regions of the brain with similar rhythmic oscillatory activity can reflect interconnectivity between neural networks and a means of connecting synaptic processes due to bottom-up and top-down cortical processing (67, 149, 150, 288). A decrease in information needing to be processed results in oscillatory pattern changes to slower rhythms, indicating that firing rates and oscillations may be coupled at the thalamocortical level (150). The rate of oscillation of waveforms is correlated with levels of wakefulness (289), with slower frequencies corresponding with sleep, coma or states under administered anaesthetics and higher oscillations reflecting resting awake or attentive states.

<table>
<thead>
<tr>
<th>Band</th>
<th>Frequency Range (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delta</td>
<td>1.5-6</td>
</tr>
<tr>
<td>Theta</td>
<td>6.5-8</td>
</tr>
<tr>
<td>Alpha 1</td>
<td>8.5-10</td>
</tr>
<tr>
<td>Alpha 2</td>
<td>10.5-12</td>
</tr>
<tr>
<td>Beta 1</td>
<td>12.5-18</td>
</tr>
<tr>
<td>Beta 2</td>
<td>18.5-21</td>
</tr>
<tr>
<td>Beta 3</td>
<td>21.5-30</td>
</tr>
<tr>
<td>Gamma</td>
<td>30.5+</td>
</tr>
</tbody>
</table>

Table 2. Oscillatory frequency bands and sub bands.
Delta band activity involves oscillations typically below 6 Hz (289). They appear during periods of sleep and are the most dominant band present during deepest stages of sleep, such as rapid eye movement (REM) sleep (149, 289). However, it is not a major component of waking state EEG in normal, healthy adults. It has been suggested to also play a role in diverting mental attention towards internal processing (290). Theta band activity constitutes approximately 5% of healthy waking adult activity and occurs between 6.5-8 Hz, and is also associated mainly with sleep (289). Both Delta and Theta bands have been suggested to be involved in diverting mental attention towards internal processing (290). Alpha band ranges are between 8.5-12 Hz (291) and account for approximately 95% of normal waking adult EEG activity when eyes are closed, and has been extensively studied (255, 256, 258). Alpha activity is especially heightened around the occipital, posterior and parietal areas. However, it becomes suppressed when eyes are opened or when doing mental tasks (289, 291, 292). Alpha activity is thought to relate to activation of the visual system in preparation for incoming visual input and also represent resting state or lack of mental activity, however the underlying mechanisms behind this are still not clear (148, 291, 292).

Frequencies between 12.5-30 Hz represent the Beta rhythm band, and this band activity is more prominent around the frontal or central scalp regions (148, 293). Beta bands display asymmetrical patterns of activation between the two cortical hemispheres in healthy waking adults (294) and this characteristic makes it distinct from other oscillatory bands. When eyes are opened, beta patterns show significant reductions in the posterior region but an increase in frontal-right hemisphere regions (256, 258). The administration of various drugs such as sedatives, antihistamines or antidepressants is also associated with heightened beta activity (256).

Gamma bands are formed by the fastest oscillations in the cortex, and refer to frequency activity greater than 30 Hz, which can reach up to around 200 Hz, but is typically, centred around 40 Hz (295). Spontaneous gamma bands signify active information extraction within the cortex (150) and propagation of information to higher levels of the processing hierarchy (295). Gamma activity levels can signify the level of consciousness of the individual, and focal gamma activity activated as part of a larger functional network may be involved in conscious perception (4, 7, 67). Synchronization of gamma-band activity present in various thalamocortical columns may bind various auditory neural activity to produce coherent auditory perceptions (149, 150, 296). Animals with missing gamma band thalamocortical pathways showed no cognitive response following sensory stimulation (151). Sound intensity
is also related to gamma band activity levels (296). Exogenous gamma activity is localized within the relevant sensory areas and is transient, normally increasing then decreasing (waxes and wanes) depending on the presence of external stimuli (289, 297). Selective attention has been linked to long-term synchronization of endogenous gamma rhythms and significant reductions in this band activity noted in patients with attention deficit disorders (295, 298). Gamma oscillations typically last approximately 25 ms; the first 10-15 ms may involve integration of incoming information and the subsequent 10-15 ms window for propagation of the input to higher levels (295). Typically, however, persistent endogenous gamma activity in a brain region can be considered pathological (67, 149).

Cross-frequency coupling between bands is also possible whereby one band can be overlaid or ‘carried’ on top of another, usually slower oscillatory band (287). The most commonly observed are phase–amplitude and phase–phase cross-frequency coupling, but amplitude–amplitude, phase–frequency cross-frequency coupling can also exist. A common transient coupling is theta-gamma coupling (147, 287) (Figure 4). In this, gamma waves are proposed to integrate information within local hubs while theta waves synchronize activity across spatially distant hubs, acting as a carrier wave (147, 299). Theta-gamma coupling has been implicated in various cognitive (147), memory (300), and auditory processing (301). Kendrick et al. (302) observed that learning alters theta-gamma coupling patterns.

![Figure 4. Schematic diagram illustrating frequency coupling of fast oscillating gamma bands (approximately 30.5-60 Hz) onto slower oscillating theta bands (approximately 6.5-8 Hz).](image)
2.4.3. Limitations and variables influencing EEG

The most obvious limitation is that activity near the scalp is recorded, and some important neuronal population activity may not be recorded due to being deep inside the cortex or without sufficient synchrony (271). Thus, activity from key sub-cortical structures such as the thalamus are most likely not recorded. Bias for neuron types are also present, pyramidal cells are predominantly recorded, and thus claims cannot be made about global brain activity (272). The dipole fields may not behave ideally and produce classic electrical fields – as discussed under the volume conduction theory, the presence of different conduction mediums may ‘smear’ signals and obscure the intracranial source, and when there are large arrays of neurons, the locus of the dipole may give the illusion of being located deeper within the cortex than the actual population (261, 303).

While the sources of activity are approximated, we can only make inferences about the underlying cognitive processes which are taking place. The inverse problem (304) is a common issue with EEG, because the sources are being estimated from scalp potential distributions, theoretically more than one solution set is possible for any given potential map (269, 271, 272). There are potentially an infinite number of sources that can give rise to the same signal but only a limited number of recording points. However, several lines of research have focused on this issue over the years and techniques are now in place to produce very close estimates of electric dipoles involved (305-309). Often, knowing in advance about the nature of potential sources (apriori assumptions) (270, 305, 308) will increase the accuracy and validity of estimates, e.g. when presenting auditory stimuli, it is generally expected that regions of the Heschl’s gyrus and superior temporal gyrus will be involved. EEG recordings are also affected by drugs which can affect brain function, and whether the participant is awake or asleep or the stage of sleep (310). An individual typically passes through five stages of sleep – I, II, III, IV and deep sleep or rapid eye movement (REM) sleep (291). Nielsen-Bohlman (310) observed that in stage II of sleep, N1 waveforms reduced while P2 and N3 amplitudes increased. As this further progressed to stages III-IV, N1 further reduced but was restored during REM sleep. These considerations should all be taken into account when interpreting electrophysiological data; nonetheless, while what is measured on the surface of
the scalp is not a direct, ideal relationship, EEG does provide valuable objective information regarding processes occurring very fast in time.

2.4.4. Tinnitus and EEG

EEG methods are becoming increasingly popular for investigating the neuronal changes associated with tinnitus (311). Tinnitus sufferers can be objectively compared with non-tinnitus controls to better understand the underlying central mechanisms giving rise to the phenomena. A key advantage is its non-invasive nature, which allows for examination of real-time human cortical activity with minimal interference to the participant. This is advantageous over animal studies of tinnitus, where findings cannot be extrapolated fully to humans and it remains difficult to assess tinnitus perception and distress (35), and invasive techniques, which pose ethical concerns and have limited applicability in mainstream settings (221). The ability to examine oscillatory band activity with EEG is beneficial considering that maladaptive neuronal functional connectivity is proposed to sustain tinnitus (312-314). Moreover, the recordings can be made in complete silence which allows for participants to still detect their tinnitus and resting-state activity to be examined (256). This is in contrast to fMRI, for example, where the scanner is considerably noisy (exceeding 100 dBA in cases) (288). When attempting to measure tinnitus activity, a key methodological concern which needs to be considered is its heterogeneity. The tinnitus population is a diverse group with different presenting clinical features (2). It is possible that clinical features can manifest from underlying functional neuronal network differences (4). There is variability in spontaneous and induced oscillatory activity within and between individuals (300); this also needs to be taken into consideration when interpreting tinnitus studies using EEG. As discussed in Section 2.2.2.2. Central Compensatory Processes, tinnitus may lead to changes in characteristic frequencies of brain wave oscillations within the cortex. As tinnitus sensation is subtle, the changes in EEG oscillatory rhythms are also likely to be relatively small in scale; therefore it is advantageous to have appropriately large sample sizes, and strong a priori assumptions and hypotheses regarding the networks which may be involved. Comparison groups need to be matched carefully in order to validate differences between the two groups. Specific tinnitus and EEG studies are discussed in Chapter 8. Auditory streaming and prediction in tinnitus sufferers.
2.5. Adaptation Level Theory Model of Tinnitus

2.5.1. Adaptation Level Theory

The Adaptation Level Theory (ALT) was formulated through the 1940s-50s (315) and then summarized by Helson (43) to conceptualize the effect of context on sensory perception and psychophysics (43, 316). The adaptation level (AL) is the body’s internal anchor or reference point. Any incoming stimulus is not processed in isolation but is compared to this reference for estimating sensory magnitude and making perceptual and discriminatory judgements. This is analogous to the concept of the brain processing incoming stimulus in terms of contrast rather than absolute values (30). In this case, contrast with the AL is determined - if the evoked stimulus sensation is weaker than the AL, it is perceived as being of low magnitude; if the sensation is larger, it is perceived as being greater. The greater the discrepancy in magnitude between the stimulus and AL, the more strongly it is perceived by the individual as being a stronger or weaker stimulus (317, 318). Moreover, the adaptation level is determined by both present and past experiences of a stimulus and is able to change over time (43, 44). Stimuli higher in level can displace the AL upwards, and vice versa. Apart from context, this internal adaptation level is also influenced by various psychological and cognitive factors termed residuals, that can either aid or counteract AL shifts (43, 319).

Residual factors can include past experiences (memory) and prediction of future events, emotions, physiological state/arousal, and personality. This intricate relationship has been described by Helson (1964) in terms of this mathematical formula:

\[ A = X^pB^qR^r \]

A is the adaptation level, which is the weighted or geometric mean of three components: X the focal stimuli (the stimuli in the forefront which are being attended to), B the background or contextual stimuli (they provide the context within which focal cues operate) and R is the sum of residual factors. It is noteworthy that some of these components are internal and some are placed external to the individual. The weighting coefficients p, q and r establish the relative contribution of each component towards the final adaptation level (p+q+r =1). These weighting coefficients can be influenced by attention and related processes. The component which is attended to at any point in time will be given greater weighting and that component will have an increased influence on setting the internal anchor. Adaptation level based judgements occur
for all incoming stimuli, regardless of whether it is in the forefront or in the background. However, focal and background components can switch if an individual swaps attention from one stimulus to another. In cases, it is also possible for the focal stimulus to become a residual factor over time (43).

In its logarithmic form, the formula can be solved using methods of multiple linear regression analysis and least-squares:

\[
A' = p \times X' + q \times B' + r \times R' + C
\]

\[
= p \times X' + q \times B' + (1 - p - q) \times R' + C
\]

\[p,q,r : \text{weighting factors} \quad p+q+r = 1\]

\[A' : \text{Logarithm of adaptation level} \quad A' = \log_e (A)\]

\[X' : \text{Logarithm of tinnitus perception} \quad X' = \log_e (X)\]

\[B' : \text{Logarithm of background sound perception} \quad B' = \log_e (B)\]

\[R' : \text{Logarithm of residual factor} \quad R' = \log_e (R)\]

\[C : \text{Constant}\]

In theory, focal, background, residual components and weighting factors can be manipulated or controlled within an experimental setting to study the resulting effect on overall AL.

In summary, the two fundamental principles of the ALT (as described by Helson) are that:

1. “Every stimulus displaces level more or less in its own direction, providing that counteracting residuals are not operative. If a stimulus is above level, the level is displaced upward; if below level, downward; and if it coincides, it does not change level” ((43), p61).

2. “The fact that adaptation level is a weighted mean of external and internal stimuli implies that the influence of one class of stimuli may be counteracted by sufficient emphasis on other classes of stimuli.” ((43), p61).

The ALT can essentially be applied to any objective stimulus (43). At present, context-dependent magnitude judgements have been illustrated in experimental studies of
proprioception, taste, phobias, olfaction, temperature, weight, and vision. Social and abnormal psychology have modelled various constructs such as aversive behaviour and traffic noise annoyance using ALT. In market research, the subjective price perceptions of consumers have been effectively conceptualized as well. Depending on the field of study, adaptation can be called fatigue, desensitization, habituation, acclimatization and stimulus failure. This can cause some confusion in terminology. For example habituation, perhaps the simplest form of learning, has found its way into the tinnitus literature while adaptation may be under conscious control to some degree and may describe more accurately some of the changes observed in tinnitus with time. Hensel derived a definition of adaptation which is most consistent with the ALT model: adaptation is either an increase or decrease in sensory response observed as a result of the fact that such systems have properties which can vary with time.

Aside from objective stimuli, empirical observations of loudness (a subjective phenomenon) and chronic pain remain consistent with the ALT. observed that in comparison to controls, patients suffering from chronic pain perceived pain stimuli - electrical stimulation in the experiment - as being less intense and less unpleasant. It is conceivable that the chronic pain patients had established a higher internal adaptation level for pain. Thereby, any external pain stimuli become relatively low in judged magnitude.

2.5.2. ALT model in relationship to tinnitus

Traditional psychoacoustic models to date have predominantly focused on perceptual characteristics of tinnitus which can be formally reported and measured, such as pitch and loudness. In many ways, these models adopt a reductionist approach such that tinnitus is studied in isolation. It is arguable that this approach is limited in understanding tinnitus, which is a dynamic phenomenon and which does not follow all the rules which apply to external sound. Searchfield et al. developed an Adaptation Level Theory (ALT) model of tinnitus perception by applying Helson’s theory to magnitude estimates of tinnitus. It is an ecological framework which takes a holistic approach to understanding the phenomenon and its complexity (Figure 5). For loud tinnitus, a high internal AL is established – thus the tinnitus is perceived as being of high magnitude. In a similar manner, the distress experienced by tinnitus can also shift based on an internal reference point, potentially driven by non-
auditory physiological mechanisms (88, 180, 330, 331). A high set-point for tinnitus AL can therefore characterize tinnitus which is not only louder but also one which can elicit greater negative emotions in an individual. The final AL magnitude estimates of tinnitus, as well as distress judgements, are derived by multifaceted interactions between the following: the focal component (tinnitus), contextual component (any background noise or applied sounds), and residual components (individual cognitive and behavioural characteristics, such as past experiences, prediction, emotion, personality traits, and physiological arousal) (5, 6, 10). In the outer environment, the physical location (e.g. bedroom, beach, loud restaurant/bar) as well as time of day can alter the magnitude of tinnitus as well. These changes can occur via influencing our attention, cognitive reserve, levels of arousal/stress, health status and emotional status and are dependent on the individual themselves (6). The environment is more dynamic than broader, slow-changing social factors such as an individual’s cultural norms, beliefs, religion, relationship and moral support and interactions with health professionals and their tinnitus management strategies. Attention and auditory scene analysis (61, 69, 164) processes are weighting factors, which help determine which component is given predominance at any time.

2.5.2.1. Focal (Tinnitus) and Background (External Sound) Components

With chronic tinnitus, the focal component remains a salient signal robust to habituation, resulting in higher weighting towards it and high AL even if the background sounds are high in volume (80). Tinnitus continues to be processed while any constant external sound is essentially tuned out by the auditory system over time (77, 78). Furthermore, this saliency can activate the non-auditory distress network, also establishing an elevated tinnitus distress AL. The tinnitus and background sound intensity relationships may differ as a function of frequency, based on the individual’s hearing loss pattern (5, 6). Within the context of sound therapy, when an external sound is introduced into the auditory system that is of lower level
Figure 5. The ecological model of tinnitus. This model consists of a psychophysical core described by adaptation level theory in which tinnitus and background sound perception are under influence of individual psychology factors classified in ALT as “residuals.” These factors are influenced by the environment and social context. The adaptation level is the weighted product of: X, the intensity of tinnitus signal, B, intensity of background neural activity, and R, intensity of residual components (e.g., memory, arousal, and personality). The weighting coefficients p, q, and r determine the relative contributions of components to adaptation level and are considered to reflect attention and auditory scene analysis. Helson (1) expressed this relationship mathematically: A=XpBqRr. Reproduced with permission from (6), pg 2.

than the tinnitus, the tinnitus AL will be reduced as there is a bias in the direction of the introduced sound (given that an appropriate level of attention is paid towards the stimulus). Subsequently, it is reduced in audibility and/or distress. If presented for a long-term, these perceptual changes can be sustained. On the other hand, if stimuli are presented at a level considerably lower than the existing AL, there may be insufficient attention paid to the external sound, therefore there is no change in tinnitus AL. An important factor of the ALT to consider is that while the adaptation level is biased towards the direction of the stimulus with prolonged stimulation, it never reaches the same sensation level of the stimulus (43). That is, the internal reference point will remain less than an intense stimulus and greater than a weak stimulus. Therefore, the tinnitus will never be completely eliminated. However, other ALT factors would also have to be considered when selecting the level and frequency for
administering sound frequency as a form of clinical treatment: individual residual factors can aid or inhibit the effects of sound therapy, etc. By applying a holistic approach to sound therapy and considering that several factors (other than physical aspects of sound itself) influence final therapy outcomes, the ALT model provides new avenues for sound therapy research and understanding of contributing factors.

The presence of an AL for tinnitus can also help explain the tinnitus loudness paradox (5, 37, 114) and the prevalent observation of significant LLM changes upon administration of treatments, with negligible subjective rating changes of tinnitus loudness (107, 108). Interpreted under ALT, the loudness paradox arises because subjective loudness judgments estimate the current tinnitus AL: it is made in a sound proof booth with no contextual noise stimuli (37, 114). In contrast, the objective match is made when an external test stimulus is introduced and the individual has to match it with the existing tinnitus AL. The addition of the external sound itself may alter the tinnitus AL, creating a new anchor point so that tinnitus is matched to an external matching sound at a lower than expected level. Moreover, it is also possible that if the external sound undergoes adaptation over longer periods of time, under the ALT framework the matching sound would be perceived as quieter; this would need to be increased even more in level before it can match tinnitus intensity. Durai et al. (10) observed that with short-term (20 minute) exposure to sounds, subjective tinnitus loudness changes were negligible. In contrast, objective loudness matches increased for the 10 dB SL and 20 dB SL conditions compared to the quiet and threshold conditions. There was no significant correlation between the two measures pre-experimentally. Hence, one interpretation for the increase in loudness level matches with increasing intensity of experimental sound might be that external sound adaptation occurred to a greater extent than tinnitus adaptation in this study.

2.5.2.2. Residuals

Residual components of the ALT model are individual cognitive and behavioural characteristics which may hypothetically influence tinnitus magnitude by biasing tinnitus AL to be set greater or less than would be in their absence. Residuals outlined in the framework include personality traits, emotional affect or state, previous experiences/memory of the tinnitus, prediction of sounds, and physiological arousal levels (45), but in theory may also encompass any relevant individual factor such as coping strategies, perceived control over
tinnitus, physical health and disability and hearing (115, 116, 117). Some residuals are innate to the individual (e.g. personality, memories) while others such as arousal are determined by the environment. Furthermore, residuals can correspond to the non-auditory neural networks outlined in physiological models relating to conscious tinnitus perception and/or distress (4, 78, 83). Essentially, from a therapeutic aim, ‘maladaptive’ residuals bias weighting towards the focal component and increase tinnitus AL. If this effect is strong enough, this may counteract any bias initiated by contextual sounds under sound therapy paradigms, resulting in no overall change. Support for this hypothesis comes from observations such as that perceived tinnitus loudness is increased upon presentation of loud or uncomfortable levels of tinnitus masking (20, 23). Although the increased weighting on contextual sounds should theoretically lead to a decrease in tinnitus audibility, the activation of strong emotional and physiological arousal residuals (elicited by discomfort to masking) (59, 196) as well as attention diversion (158) can prevent overall shifts in AL. Other ‘maladaptive’ residuals which prevent AL shifts may include negative associations or memories of tinnitus, stress or anxiety, learned helplessness, and utilization of maladaptive coping strategies (6). In contrast ‘adaptive’ residuals elicit added benefit in interventions by lowering AL. Residual effects can be strong or minimal, and various residuals can interact within themselves in complex ways (45). The amount and direction of effect of residuals may be dependent on various higher-level individual factors, such as the individual’s signal detection criterion (74).

2.5.2.3. Attention and Tinnitus

Attention broadly refers to the ability or power to concentrate mentally (332). Literature distinguishes two types of attention: automatic (unconscious) and controlled or selective (conscious) attention (128). Humans can selectively attend to specific sounds and ignore others arriving simultaneously (8, 128, 157, 158). In particular, novel or biologically significant sounds are preferentially attended to and processed with greater ease in the auditory system (potentially as a result of neural gain change, see “Mechanisms of ALT: Gain Control and Loudness Adaptation section” below) (8, 158). De Ridder’s (78) heuristic model states that in order for tinnitus to be consciously perceived, it needs to be paid attention to – a process involving coupled activity between salience and perceptual tinnitus networks (78). There can be difficulty further inhibiting or habituating to this signal (182).
Individuals placed in a silent (high salient) environment often experience tinnitus-like symptoms which were not previously present (101). Knobel & Sanchez (158) observed that shifting attention away from the tinnitus by getting the individual to do visual attention or movement cognitive tasks leads to a significant decrease in tinnitus audibility (from 68.2% to 45.5% and 19.7% respectively), while background sound was kept constant. Tinnitus sufferers have shown slower reaction times and increased error rates on various selective attention tasks compared to matched controls (2, 158, 333-336). The general depletion of resources theory (335) accounts for this observation as that cognitive resources are directed towards the tinnitus signal, therefore there is less cognitive reserve left to carry out the tasks. Current psychological therapies using attention, such as attention training or attention diversion therapy, operate via shifting the individual’s focus away from the tinnitus and have demonstrated effectiveness (20). Wise et al. (333) observed benefits in applying a game-based attention training method specifically targeting selective attention for tinnitus patients.

Attention may dictate which components are given significance and determine the final AL set-point. The ALT model terms Orientation as the extent to which an individual attends to a change in the stimulus itself (5). It should be noted that this definition is not analogous to definitions of orientation as an attention subsystem used in traditional attention models (e.g. (337)). Large discrepancies between stimulus and adaptation level result in greater orientation (43, 45) (Figure 6). For these stimuli, any further change also becomes more noticeable. Ideally, the lowest possible orientation possible is preferred so that any change in the tinnitus perceptual magnitude is not attended to, thereby preventing shifts in AL.

2.5.2.4. Auditory Scene Analysis and Tinnitus

Auditory scene analysis (ASA) is the process whereby incoming sounds are organized by the auditory system into acoustic objects (e.g. car horn, telephone ring) or streams of sounds (e.g. voice of someone speaking, musical melody) (61, 68-70). A knowledge of the “what” and “where” is generated as a result of ASA. ASA is often divided into two stages (69, 338). The first stage of primary signal segregation is largely stimulus driven and involves encoding the main auditory features of incoming input, such as pitch, timbre, loudness (69, 164). The second stage of ASA is heavily influenced by top-down influences involving a combination of attention, intention and schemas of past experience (61, 65, 69, 339, 340). Gestalt principles (69) such as similarity (sounds similar in acoustic features are more likely to be
emitted by the same source) and continuity (sound sources often have smooth variations over time rather than abrupt changes) may be involved in perceptual decision making for grouping

**Figure 6.** (A) The theoretical relationship between orienting response/orientation (OR) to tinnitus in a background sound B as a function of different tinnitus adaptation levels (ALTIN1, ALTIN2, ALTIN3). The curves represent signal distribution. The OR is greater to the more audible tinnitus (OR ALTIN2). An increase in background sound level (horizontal arrow) should reduce orientation to the tinnitus. (B) The theoretical relationship between orientation and attention, illustrated by the orienting response (OR) to tinnitus before (top curve) and after (bottom curve) attention training. Less focus on tinnitus should reduce the strength of OR to tinnitus. Reproduced with permission from (45), p. 6.
sounds (70, 164, 340). Attention is highly intertwined with ASA (164, 340). Carlyon (341) observed an inability to separate out two frequencies played into one ear among individuals diverted by simultaneous cognitive tasks (e.g. counting backwards). However, when the two frequencies were attended to, they were effectively discriminated. Limited attention and/or switching of attention can significantly influence the detection of, selective processing and following over time of an auditory object (329).

External sound and tinnitus may undergo similar processing within the auditory system, such as adaptive feature extraction, schema, and semantic object formation (5, 43). Griffiths & Warren (329) proposed four general principles of auditory object analysis that may also be applied to analysis of tinnitus:

1. Analysis of information from the sensory world
2. Separation of auditory object (tinnitus) from sensory world
3. Extraction and generalization of sensory information within the same dimension (audition)
4. Generalization between senses

Psychoacoustic matching of the tinnitus signal is possible clinically: tinnitus usually has discrete frequency, intensity, bandwidth and timing characteristics (20, 113). Furthermore, tinnitus can vary systematically in loudness and/or frequency under certain situations (e.g. time of day, stress) (342). For intermittent tinnitus, there is a distinct onset and offset perceived. In the majority of cases, tinnitus also has a location in 3D space (74). These are features which are similar to those extracted from external sound during early stages of ASA. Moreover, tinnitus can become so robust as an acoustic object that it is heard distinctly separately from sounds in a person’s environment, and in cases may be resistant to masking by external sounds (42). It therefore appears to follow the 1st and 2nd principles of object analysis accordingly. However, discrepancies may arise in the later stages of processing (3rd and 4th principles) when assigning tinnitus as a true auditory object (5, 6). As a phantom sound, there is no stored context, schema, meaning or explanation for the tinnitus: it cannot be assigned a source fitting in with any given soundscape (sounds relating to any particular environment) (40, 41). Tinnitus does not interact with external sounds in typical ways, as observed in psychoacoustic masking studies (36, 37, 39). It is highly likely that interference occurs via informational masking at higher levels of the sensory hierarchy than conventional masking (38). Finally, generalization is difficult as there is also no concurrent information
arriving from other modalities, such as vision and/or touch, which can be used to corroborate and identify a sound source (343). Auditory object processing is unable to continue efficiently as a result of the conflict between tinnitus and the expected principles followed by auditory objects. These discrepancies can drive saliency of the tinnitus signal (4, 78), establish negative reactions (45, 344) as well as prevent habituation.

2.5.2.5. Mechanisms of ALT: Gain Control and Loudness Adaptation

Tinnitus may initially be processed in a similar manner to external sound by the hearing system (5, 6). By understanding how short-term and long-term adaptation of the central hearing system to external sound occurs, it may be possible to postulate how tinnitus AL shifts may also occur over time. Gain control and loudness adaptation are both driven by changes in underlying neural firing response. Mammals can hear highly accurately over the vast range of sound levels present under natural listening conditions (345). In humans, there is a 12 fold increase in intensity of sound between the threshold of hearing (approximately 0 dB SPL) and maximum hearing limits (120 dB SPL) (346). However, across this range the firing rates of individual neurons are observed to increase only over a very limited portion of the full range of hearing - the majority of primary auditory nerve fibres firing rates only produce a dynamic range of about 35 dB (347, 348). This has been termed the ‘dynamic range problem’ (345).

Gain control is proposed as a way of compensating for this physiological limitation (134). Gain refers to the steepness of the curve in an input-output sound function of a neuron (135). Within the auditory system, the dynamic range of firing of neurons can essentially remain constant, but the level of sound covered by this range will alter based on where an anchor or gain adaptation point is set (134). Stimulus-specific adaptation effects have been observed at all levels of the auditory system from early auditory encoding (320) to the auditory cortex (135, 349) (Figure 7). Dean et al. (350) observed that in guinea pigs, individual neurons in the IC adjusted their neural firing to optimize stimulus characteristics such as the mean, variance and bimodality of the most frequently occurring sounds (the current context or acoustic environment). The neuronal regions corresponding to the frequencies which were most coded over time were termed the high-probability region (HPR) (135). For most of the neurons, rate-level adjustments occurred very rapidly with a mean time of 160 ms upon increasing incoming stimulus levels (351). Dean et al. (350) also observed a slower adaptation, occurring over a
Figure 7. Illustration of mechanisms of auditory gain control that operate at multiple levels of the auditory system (in this example, for when an animal is alerted by a novel sound). Clockwise from bottom right: (A) The anatomy of the outer ear boosts and modifies spectral cues, including those for source location (B) membrane responses of cochlear outer hair cells amplify vibrations of the basilar membrane (C) rapid adaptation of responses of midbrain neurons to match neural output based on statistics of the incoming sound (D) Cortical adaptation in response to loud sounds preserves sensitivity to quiet sounds — such as the approach of a second tiger (E) cortical facilitation of neural response functions to match incoming sound frequency/level (F) medial olivo-cochlear efferents alter rate-versus-sound-level functions to increase output dynamic range for the representation of discrete signals (tiger) within background (environmental) noise. Reproduced with permission from (135), p. 405.

Period of tens of seconds in 36% of neurons. One evolutionary advantage of this may be to track broad background level over time, so that the adapted rate level function always covers this range and thus not have to be instantly adjusted. This can also drive long-term firing response changes at the neural level (5).

Loudness adaptation refers to the decrease in perceived loudness of a steady tone (typically below 40 dB SPL) over time (352, 353). This occurs at several levels of the auditory pathway and may occur following hearing loss to reduce background noise and pick up sudden quiet
sounds (350, 351, 354). There are two types of loudness adaptation: natural (occurring spontaneously) and induced (purposely presenting a continuous tone) (353, 354). Induced loudness adaptation of a tone was found to occur at suprathreshold levels by presenting a stimulus simultaneously with a test tone, either in the same or in the opposite ear (354). Loudness adaptation can reflect underlying changes in neuronal gain, however, the issue arises in that auditory gain control would theoretically result in increased gain with the presence of suprathreshold sound; however, loudness adaptation decreases with increasing stimulation level. There is a large amount of variability among individuals in terms of how much loudness adaptation they experience (355), suggesting that higher-order psychological factors may also play a role. It is possible that neuronal gain change is also driven by top-down behavioural and other non-sensory influences (135). The perception of loudness in general is influenced by alertness and top-down attention effects (356), as well as by emotion. The same auditory stimulus may be reported as being louder, more negative and fear-inducing when conditioned with an aversive experience, compared to when it is presented alone (357).

In a study by Fritz et al. (358), ferrets were trained to perform auditory detection tasks (detect when a pure tone was played in place of a broadband sound). Enhanced localized gain was observed for frequencies similar to the pure tone administered during the detection task. These changes occurred quickly and lasted for several hours in some cases; moreover, better performance on detection tasks correlated with larger changes in the gain and shape of receptive fields. Gain is also affected by the nature of the task itself (e.g. discrimination vs. detection) (359) and the difficulty of the task (360). Hui et al. (361) observed that alterations to receptive fields in the primary auditory cortex were present in order to represent sounds which have behavioural significance, such as brain stimulation which results in rewards. Central feedback loops, e.g. the medio-olivocochlear system (MOCS) which feedback to outer hair cells, have been implied in having top-down control over gain adaptation at lower levels of the processing hierarchy, and may allow for extra gain to be provided to salient or important signals (362, 363).

Under the ALT framework, changes in cortical gain control may allow for tinnitus AL shifts to occur with changes in contextual noise, but also driven by context based on prior experience, learning and reward and relevance of the sound. Tinnitus changes following sound interventions can be similarly modelled as induced loudness adaptation effects, reflecting
slower neural gain adaptation and that is also affected by behaviour and top-down feedback (e.g. residuals, attention, ASA) on sensory processing.

2.5.3. Purpose of Current Research

Although Helson’s model would be viewed as ecological in today’s terms, the ecological model of tinnitus more explicitly states its holistic approach and adaptation level at its core. Tinnitus is viewed as an auditory object and not merely as a sound signal, and the model stresses active interaction between an individual experiencing tinnitus, cognition and their environment. The ALT framework is compatible with several current tinnitus observations and experimental findings. This coherent framework can unify existing physiological, psychological and psychoacoustic models of tinnitus in order to solve some of the existing gaps in knowledge (6).

As the model is based on a mathematical formula, it is theoretically possible to calculate optimal parameters or foci for intervention. If correct the model serves a very useful function as current mechanisms are unable to fully account for how individual variables may affect tinnitus treatment outcomes. Multidisciplinary approaches are often utilized in the hope of finding an approach which best works for an individual – eliciting a trial and error approach, which may be time-consuming and dishearten or stress individuals over longer periods of time.

Preliminary studies have been conducted specifically applying the ALT model. However, these have predominantly examined the relationship between tinnitus and contextual sound (10, 364). Durai et al. (10) administered NBN for twenty minutes in quiet and increasing sound levels. Tinnitus distress interacted with contextual noise levels in a manner consistent with the ALT model, with higher volume of background sound resulting in lower distress ratings. Tinnitus loudness ratings did not change. It was possible to observe an emergence of ‘adaptation-sensitive’ and ‘adaptation-insensitive’ individuals. An adaptation-sensitive individual may be able to have tinnitus magnitude change in the presence of background and/or residuals as predicted by the ALT model, whereas for adaptation-insensitive individuals, tinnitus magnitude is not susceptible to change. Whether this finding will hold in future studies remains debatable as this was a single examination. An interaction between the personality traits of social closeness, positive emotionality, stress reaction and negative emotionality and contextual noise effects on tinnitus was also observed. Individuals with high social closeness (and high positive emotionality) experienced an increase in subjective tinnitus loudness and distress under the presence of contextual noise. Individuals with low
stress reaction (and low negative emotionality) had an increase in objective tinnitus loudness matching with contextual noise.

The ALT model of tinnitus is in strong need of further empirical investigation, particularly with regards to which residuals show a relationship with tinnitus, and their systematic interactions with the phantom sound perception. These residuals can potentially exert a robust top-down effect on tinnitus signal processing. Understanding how personality traits, emotion, prediction and memory, tinnitus and background sound all interact as components of the ALT could lead to more effective and efficient treatments for tinnitus.
Chapter 3. Anxiety and Depression, Personality Traits Relevant to Tinnitus: A Scoping Review
3.1. Preface

Publication

This chapter includes content from the article “Anxiety and Depression, Personality Traits Relevant to Tinnitus: A Scoping Review” published in the International Journal of Audiology (2016), 55(11), 605-615.

What was undertaken?

Scoping reviews of existing literature were conducted to identify key personality traits relevant to tinnitus, and examine the relationship between affective disorders and tinnitus. Sixty studies were chosen for charting the data, 14 studies examined personality traits exclusively, 31 studies examined affective disorders exclusively and 15 studies investigated both. Personality traits were found to have a consistent association with the distress experienced by adult tinnitus help-seekers, and help-seekers were also more likely to experience anxiety and depression symptoms and/or disorders.

Why was this needed?

It is not fully understood why some individuals adapt to their tinnitus and why others do not. Certain personality traits and psychological disorders, especially depression and anxiety, often coexist with tinnitus and may act as predictors for tinnitus severity. These scoping reviews were conducted in order to map all the existing literature on personality traits, affective disorders and tinnitus without critically appraising the quality of individual studies. This is particularly useful when the topic is complex or has a heterogeneous nature, such as tinnitus, and enables for studying the nature and extent of psychological influences on tinnitus, as well as identifying any research gaps in the existing literature.

How did it contribute to the objectives of the PhD?

Personality traits are one of the residual factors under the ALT model of tinnitus which may work in a top-down manner to influence tinnitus magnitude and distress judgements. While specific personality traits were identified as being associated with tinnitus perception and distress in this review, further research in this area needs to look at controlled comparison of personality trait profiles of tinnitus sufferers and non-tinnitus individuals (by matching for other variables such as age, gender, degree of hearing loss, etc.). Also, the existing literature
has predominantly examined tinnitus loudness and distress associations with personality. It would be of interest to examine the relationship between key traits and various perceptual tinnitus characteristics such as pitch, location, or tinnitus changes to loud sounds. This will also allow key personality traits to be modelled under the ALT framework. These limitations were addressed by administering a web-based personality, tinnitus and hearing survey to tinnitus sufferers and a non-tinnitus control group (Chapter 4).
3.2. Abstract

**Objectives:** Scoping reviews of existing literature were conducted to identify key personality traits relevant to tinnitus, and examine the relationship between affective disorders and tinnitus.

**Study Design:** The methodological framework of Arksey & O’Malley (365) was followed. Sixty studies were chosen for charting the data, 14 studies examined personality traits exclusively, 31 studies examined affective disorders exclusively and 15 studies investigated both.

**Results:** The presence of one or more specific personality traits of high Neuroticism, low Extraversion, high Stress Reaction, higher Alienation, lower Social Closeness, lower Well-Being, lower Self Control, lower psychological Acceptance, presence of a Type D Personality and externalized Locus of Control were associated with tinnitus distress. Anxiety and depression were more prevalent among the tinnitus clinical population and at elevated levels.

**Conclusions:** Personality traits have a consistent association with the distress experienced by adult tinnitus help-seekers, and help-seekers are also more likely to experience affective symptoms and/or disorders.
3.3. Introduction

Tinnitus is the perception of sound by an individual in the absence of an external sound (2, 20, 34, 86). While 4-32% of the general population is thought to have constant tinnitus, it is only a subgroup of 15-20% of the tinnitus population who are distressed by it (11, 12, 95, 366). Distressing or severe tinnitus is commonly characterized by one or more symptoms of disturbed sleep and concentration, problems with hearing, disruption to everyday activities, irritation and annoyance, anxiety and depression (13). It is not fully understood why some individuals adapt to their tinnitus and why others do not (21). All of the distress caused by tinnitus is not explainable by its psychoacoustic characteristics (21, 367). A large body of literature now suggests that psychological variables play an important role in tinnitus perception and distress (5, 6, 13, 20, 21, 53). Certain personality traits and psychological disorders, especially depression and anxiety, often coexist with tinnitus and may act as predictors for tinnitus severity (368, 369).

The term ‘personality’ defines an individual’s typical thoughts, actions, behaviours and interaction style (46, 48). The trait theory developed by Allport (370) states that personality is composed of a set of broad dispositions or traits. Each trait is a dimension which lies in degrees along a continuum, and can be measured using self-report questionnaires (370-373). Two popular personality trait models are Eysenck’s three dimensional model (371) and the five factor model (FFM) (372). Neuroticism and Extraversion traits are common to both models, and describe the tendency of an individual to experience negative emotions and the tendency to exhibit sociability, assertiveness and express emotion respectively. In the tinnitus population, high Neuroticism and low Extraversion has been often been reported (93, 374, 375). High Stress Reaction and low Social Closeness has been associated with tinnitus (167). Bartels et al. (93, 376) also concluded that the presence of a specific Type D Personality (defined by a cluster of personality traits describing a greater tendency to experience negative emotions and social inhibition) is correlated with tinnitus distress levels. On the other hand, an internal Locus of Control (367, 377) and the trait of Acceptance (378) have been linked with reduced tinnitus distress. It is of interest to examine these associations and also see if there are other personality traits more prevalent among tinnitus sufferers than non-tinnitus individuals.
Personality traits (temperamental) are robustly related to mood and anxiety disorders (176, 379, 380). This association can occur in many ways, and the direction of this relationship is not entirely clear (47, 51). Depression and anxiety have been reported to be more common among tinnitus sufferers, although this is a grey area with some contradictory findings (381-386). One key limitation may be due to the fact that the symptoms of distressing tinnitus have considerable overlap with that of depression (369), and this would elicit errors in terms of overestimating the symptoms of both when attempting to measure the two in a single study. It is anticipated that charting the available data in detail will enable us to gain a clearer understanding of the relationship between anxiety and depression and tinnitus, and better estimate prevalence.

It was of interest to obtain an overview of all the studies which have been conducted in order to see the nature and extent of psychological influences on tinnitus. Therefore a scoping review design was selected. Scoping reviews using Arksey & O’Malley’s (365) methodological framework are designed to: “examine the extent, range and nature of research activity, to determine the value of undertaking a full systematic review, to summarize and disseminate research findings and to identify research gaps in the existing literature” (365, pg 21). This is a narrative account of existing literature on the topic.

The research questions are:

1. What personality traits are related to tinnitus perception and distress in adult sufferers?
2. What is the relationship between tinnitus and affective disorders in adult sufferers?

### 3.4. Methods

The Arksey & O’Malley scoping review methodology was followed in conducting this literature scoping review (365). The key words: *tinnitus AND personality traits, tinnitus AND personality, tinnitus AND psychiatry, tinnitus AND affective disorders, tinnitus AND psychology* were extensively searched on four databases: PubMed, Scopus, SpringerLink and PsychInfo. From the initial search results, the top four common journals from which articles were published were also hand searched (Audiology, Journal of Psychosomatic Research, Journal of Personality and British Journal of Audiology). Reference lists of articles were
reviewed to identify any further relevant studies. Ninety-seven articles were short listed based on title relevance. After reading the abstracts, and applying the exclusion criteria (minimum age of participants less than 18, or article not available in English), 60 studies were chosen for charting the data. The literature was then organized thematically, according to different study types (review, intervention studies: surveys, etc.).

Fourteen studies examined personality traits exclusively and 31 looked at affective disorders exclusively. Fifteen studies investigated both personality traits and affective disorders – these studies are reviewed twice, once under each section. Personality trait studies consisted of 20 questionnaire studies, 4 experimental studies and 5 review articles. Traits judged as being contextually similar, although labeled differently, were grouped together under a common term (the term which appears most frequently in studies). Among the charted affective disorder articles, 41 were research studies and 5 were reviews. Nine studies employed structured psychiatric interviews adopting the DSM criteria for formal diagnosis of anxiety and/or depression, while the remaining examined elevated symptoms of anxiety and depression (such as questionnaire scores) without diagnosis.

3.5. Results

The results of the scoping review are divided into two sections, the first examining personality trait findings and the second section affective disorders.

3.5.1. Personality Traits

The main personality traits which this scoping review found were:

1. Neuroticism (FFM): tendency of an individual to experience negative emotions (372)
2. Extraversion (FFM): tendency to exhibit sociability, assertiveness, emotional expressiveness and excitability (372)
3. Agreeableness (FFM): low competitiveness, low self-centeredness, and less susceptibility to anger (372)
4. Stress Reaction: Tendency to experience frequent and intense negative emotions, including anxiety, distress, and anger; overacts to minor events (48)
5. Social Closeness: sociable, likes people, and turns to others for comfort (48)
6. Self Control: reflective, cautious, careful, rational; not impulsive (48)
7. Alienation: Views the world in malevolent terms; expects mistreatment and betrayal; feels a victim of bad luck (48)
8. Well-Being: happy, cheerful disposition; feels good about self; and sees a bright future (48)
9. Acceptance: more positive and open frame of mind, do not ruminate on past experiences and have a motivation to carry on with their life (387)
10. Anxiety Sensitivity: tendency to fear anxiety related symptoms (bodily signs such as increased heart rate, sweating, muscle tension, headaches, etc.) (388)
11. Type D Personality: greater tendency to experience negative emotions (negative affectivity) and are unlikely to express their emotions to others (social inhibition) (389)
12. Locus of Control: external vs. internal, whether an individual believes that they are in control of their symptoms or not in control (390)

3.5.1.1. Questionnaire Studies

**FFM Extraversion, Neuroticism, Agreeability**: Rizzardo et al. (374) and Bartels et al. (93) found significantly lower levels of Extraversion and higher Neuroticism among tinnitus patients presenting at a medical clinic. Three studies (375, 391, 392) examined Neuroticism exclusively in different population groups and found significant positive correlations between high Neuroticism and greater tinnitus distress. In contrast, Kearney et al. (382) observed no difference in levels of Extraversion or Neuroticism between tinnitus and non-tinnitus controls. After controlling for the presence of depressed mood, Langguth et al. (393) concluded that Agreeability, but not Neuroticism and Extraversion, was significantly associated with tinnitus distress.

**Social Closeness, Stress Reaction, Self Control, Alienation, Well-Being**: Greater levels of denial, irritability, lower affective inhibition (374) and more social inhibition, lower emotional stability (93) has been reported among tinnitus patients compared to control groups. Higher Stress Reaction levels differentiated tinnitus patients seeking professional help from non-help-seeking tinnitus participants in the general population, after controlling for hearing loss (367).
Among 32–year-old individuals, Welch & Dawes (167) observed those who perceived tinnitus had significantly lower Social Closeness, higher Stress Reaction, higher Alienation and lower Self Control than those who did not. Higher tinnitus severity was associated with lower Social Closeness and lower Well-Being among participants, and higher Stress Reaction and Alienation among men only. Lower levels of Well-Being was reported by Sirois et al. (377) for participants who believed that they had less control over their tinnitus symptoms and health in general.

**Type D Personality:** A Type D Personality was independently associated with tinnitus, after controlling for other personality traits (93). A further study found that Type D Personality was present in 35.5% of participants and acted as a predictor of tinnitus distress (376), with its effects on tinnitus mostly mediated by the symptoms of anxiety and depression also present in the individuals.

**Perfectionism:** While mean perfectionism scores were within normal population limits, perfectionism subscales of Personal Standards and Organization significantly predicted levels of tinnitus distress in males and females respectively (394).

**Optimism:** After controlling for age and duration of tinnitus, Andersson (395) observed significant negative correlations between levels of Optimism and measures of tinnitus related distress.

**Anxiety Sensitivity:** A study of tinnitus patients by Kleinstäuber et al. (396) found Anxiety Sensitivity to be significantly positively associated with tinnitus distress and with depression and anxiety symptoms. Fear avoidance was a key cognitive mediator in the relationship between Anxiety Sensitivity and tinnitus severity.

**Locus of Control:** Gerber et al. (381) did not find a relationship between Locus of Control and tinnitus severity among male patients presenting at a medical centre. This is in contrast to three other studies (180, 377, 397) which concluded that within a clinical setting, those with internally placed Locus of Control were significantly likely to experience lower tinnitus distress than those with an externally placed locus. Locus of Control may exert its effects on tinnitus indirectly through influencing anxiety and depression (180). Scott et al. (21) calculated that Locus of Control and individual coping ability together accounted for 37% of variability in tinnitus distress. Attias et al. (398) measured greater externalization of Locus of
Control among young, male active army personnel seeking help for their tinnitus in comparison to personnel who were not interested in treatment.

3.5.1.2. Experimental Studies

**FFM Neuroticism, Extraversion:** Wood et al. (399) injected Lidocaine (100 mg) intravenously for 30 seconds in participants with debilitating tinnitus who did not respond to other treatment techniques such as sound therapy, hypnosis, biofeedback, etc. Higher levels of Neuroticism and lower levels of Extraversion were present in participants who experienced reduced tinnitus perception following Lidocaine administration compared to treatment resistant individuals - however a statistical analysis was not conducted.

**Stress Reaction:** Heinecke et al. (400) reported that while physiological stress reactivity (measured using electromyography) was only marginally different between tinnitus and healthy control groups, tinnitus patients reported greater subjective strain (measured using questionnaires) during tests.

**Acceptance:** The Activity Engagement component of Acceptance fully mediated the relationship between initial tinnitus distress and depression and quality of life at 7 months follow-up in a longitudinal study (378). Hesser et al. (401) observed that the frequency and peak levels of Acceptance related behaviour during the second session of Acceptance Commitment Therapy (ACT) significantly predicted the level of tinnitus distress reduction six months after treatment.

3.5.1.3. Reviews/Theoretical Frameworks

Literature reviews reporting on personality traits and tinnitus have concluded that individuals who report more distressing tinnitus are also likely to display the following: greater Fearfulness or Anxiety Sensitivity, lower Acceptance and an external Locus of Control (20), a Type D Personality, high Neuroticism, low Extraversion, low Acceptance and higher Anxiety Sensitivity (13). Greater fearfulness at the onset of tinnitus was associated with greater anxiety and greater distress 6 months later (20). Belli et al. (368) state that an individual who perceives tinnitus also has a greater chance of displaying higher impulsivity, hostility, anxiety for health, emotionality and suicidal tendency.
Anderrson & Westin (53) differentiate between moderators, which directly influence tinnitus distress, and mediators, which influence distress via some other variable. Personality traits are potential moderators, while Acceptance may be conceptualized as a mediating factor. The Adaptation Level Theory (ALT) model of tinnitus (5) proposes that personality traits can act as a residual factor, and work in a top-down manner to influence tinnitus magnitude and distress judgements.

3.5.2. Affective disorders

3.5.2.1. Questionnaires

**Depression Only:** Six studies observed significant positive associations between depression state levels and tinnitus severity, within clinical settings and within the general population (21, 104, 397, 402-404). Greater levels of depression also differentiated tinnitus patients from those without tinnitus (400). In contrast, stronger beliefs about the controllability of health and tinnitus symptoms was related to lower depression (377). A large sample (n=6215) prospective study undertaken by Hebert et al. (405) over two years reported tinnitus severity also reduced when there was a reduction in depressed mood; tinnitus prevalence was reduced but to a lesser degree. Depression levels predicted tinnitus distress more strongly than hearing loss.

In terms of prevalence, 36.1% of patients in a tinnitus self-help group reported experiencing feelings of depression (17). Twenty-seven percent of tinnitus patients in Folmer et al.’s (403) study reported current depression. Pre-tinnitus onset ratings of depression (11%) were lower than post-tinnitus onset ratings (39%) among members a tinnitus self help group; however statistical analysis was not conducted (406).

Individuals with severe tinnitus can also display difficulty with masking of their tinnitus (397, 404). Andersson & McKenna (407) derived a U-shaped relationship between depression scores and minimum masking level (MML) characteristics of tinnitus patients, with low and high depression scores resulting in higher MMLs than medium scores. This is explained in terms of a diathesis stress model, whereby a 'vulnerable person' of certain psychological characteristics may become bothered by even low degree tinnitus.
**Anxiety Only:** Bayar et al. (408) recorded higher levels of hysteria among female tinnitus patients compared to non-tinnitus controls. Lee et al. (409) found no direct effect of anxiety tendencies or trait anxiety on tinnitus severity in a clinical setting - anxiety influenced cognitive behaviour (such as catastrophic interpretation and dysfunctional beliefs) which in turn corresponded with levels of tinnitus distress.

**Depression and Anxiety:** Two studies concluded that depression and anxiety psychological scores of tinnitus patients remained within the normal population range (381, 410) while one study found heightened trait anxiety and depression within tinnitus self-help group members (386). Collet et al. (384) obtained significantly higher than normal depression and hysteria scores in males only when testing new tinnitus referral patients. Rizzardo et al. (374) reported a divergence into two clusters of tinnitus patients seeking medical treatment: Cluster 1 (had greater depression and anxiety, greater tinnitus distress) and Cluster 2 (normal range psychological scores). Seventy-one percent of participants self-reported experiencing debilitating psychological symptoms after the onset of tinnitus in contrast to 50% before tinnitus onset. Among patients with hearing loss, Rutter & Stein (411) observed significantly higher anxiety and depression among tinnitus perceivers than those with no tinnitus. In contrast, Kearney et al. (382) concluded there was no difference in depression or anxiety between tinnitus perceivers and non-tinnitus controls. Tinnitus severity was also significantly positively associated with anxiety and depression within a clinical setting in three studies (180, 383, 412). Significant positive correlations were present between depression, hysteria and tinnitus loudness and distress measured using multiple scales in one study (413), while another study found low statistical correlation observed between anxiety and tinnitus distress (0.28) and depression and tinnitus distress (0.32) (386). Individuals who demonstrated psychological disturbances within the first four weeks of tinnitus onset were more likely to develop distressing chronic tinnitus (414). Low coping tinnitus patients had significantly higher depression and anxiety present – this group displayed a similar psychological profile to chronic pain patients (415). Elevated depression, anxiety and tinnitus loudness was present among help-seeking tinnitus sufferers than non-help-seeking male active army personnel (398).

**Hearing Loss and Other Factors**

Several studies also investigated the effect of other factors/variables on the relationship between anxiety, depression and tinnitus (385, 413, 416). Meric et al. (413) observed that
degree of hearing loss was significantly associated with hysteria levels. Anxiety and depression reports were more common among tinnitus patients than in normal hearing or slight hearing loss controls (416). Reich et al. (385) recorded significantly higher levels of depression and hysteria among patients presenting with tinnitus as the main complaint in a clinic, when compared to those with hearing loss as the main complaint. The presence of depression and hysteria in males tinnitus patients in a clinical setting also correlated significantly with the presence of hearing loss (384). Rutter & Stein (411) concluded that anxiety and depression levels were not significantly different between tinnitus patients with hearing loss and other ENT patients with non-otological problems (such as nasal obstruction and/or bleeding, voice hoarseness or nasal polyps) – both groups displayed higher levels than patients with hearing loss only. After controlling for hearing loss in a study by Scott & Lindberg (367), anxiety and depression levels were significantly higher among treatment seeking tinnitus patients compared to non-help-seekers or those without tinnitus. When various covariates such as low self esteem and Well-Being were adjusted for, only a weak association existed between anxiety and depression and tinnitus in the general population (417). Fear avoidance was significantly correlated with tinnitus severity and with depression and anxiety symptoms, however, it did not seem to mediate the relationship between depression and anxiety and tinnitus distress (396).

### 3.5.2.2. Diagnostic Interviews

The following were studies that employed structured psychiatric interviews adopting the DSM criteria for diagnosis.

Using clinical interviews House et al. (418) observed that tinnitus patients displayed 1 of 3 reactions to the tinnitus: a depressive reaction (36%), a hysterical reaction (41%) or conversion reaction (schizophrenic symptom and character disturbances) (23%). Depressive reaction patients improved the most with psychotherapy and biofeedback therapy. O’Connor et al. (391) concluded in their study that 9.5% of tinnitus patients suffered from severe depressive illness, while 33.3% had affective disorders of some sort. Of 77% of tinnitus patients at an ENT department who met the criteria for diagnosis of a psychiatric condition, 29% had anxiety disorders and 26% had affective disorders (419). Sixty-two percent of tinnitus patients in another study had history of lifetime depressive disorder, 29% had current depressive disorder and 45% experienced anxiety disorders – 7% of patients (420). In a
similar study by Holgers et al. (421) 62% of tinnitus patients with hearing loss up to a mild
degree had a history of a lifetime depressive disorder, 39% had current depressive disorder
and 13% had an anxiety disorder. Thirty percent of cases had both depressive illness and
anxiety coexisting, and for 90% of the patients with depression/anxiety, the onset of disorders
happened before or simultaneously with tinnitus onset. Two studies recorded significantly
greater lifetime depression prevalence for tinnitus patients than controls with hearing loss and
no tinnitus: 62% vs. 21% (422), 78% vs. 21% (423) and significant higher prevalence of
current depression for tinnitus patients than controls: 48% vs. 7% (422), 60% vs. 7% (423).
When tinnitus patients seeking treatment were compared against control participants from the
community, 26.7% of the tinnitus group had at least one psychiatric diagnosis compared to
5.6% in controls, anxiety disorders being the most common diagnosis (424). Erlandsson &
Persson (425) found that 25% of tinnitus patients seeking treatment had average or above
average anxiety and depression. A subgroup from this set were further interviewed, and 50% diagnosted with a personality disorder - those patients with personality disorder experienced
more changes in tinnitus distress over 18 months follow-up.

3.5.2.3. Literature Reviews & Theoretical Frameworks

Literature reviews conducted on the topic have summarized that elevated anxiety and
depression levels are present and affective disorders are more common among tinnitus
patients in a clinical setting (368, 426, 427). Tinnitus patients presenting at hospitals might be
a subgroup of the larger general tinnitus population, with intensive symptoms. Psychological
factors such as depression seem to predict tinnitus severity more than psychoacoustical
measurements, and should be taken into consideration during initial clinical assessments of
tinnitus (428). Langguth et al. (369) discussed common neural pathways by which depression
and tinnitus might mutually interact.

3.6. Discussion

3.6.1. Personality traits

Neuroticism and Extraversion in the FFM have traditionally been thought to have the greatest
associations with tinnitus. Five out of 7 studies examined in this scoping review found a
positive relationship between high Neuroticism and greater tinnitus distress, and 2 of the 5
studies concluded that lower Extraversion was associated with greater tinnitus distress. However, other less commonly discussed personality traits also showed significant relationship with tinnitus perception and/or distress, such as high Stress Reaction, Lower Social Closeness, lower Self Control, lower Well-Being and higher Alienation. High Anxiety Sensitivity and low Optimism positively correlated with levels of distressing tinnitus. In contrast, greater levels of Acceptance and Acceptance related behaviour may facilitate tinnitus distress reduction in the long term. Four out of 5 studies reported an external Locus of Control to be significantly associated with greater tinnitus severity. A higher Type D prevalence was also found among tinnitus sufferers; this appears to be an indirect relationship mediated mainly by symptoms of anxiety and depression. While overall trait perfectionism was not associated with tinnitus distress, certain subscales of perfectionism significantly predicted tinnitus distress for males and females. The literature reviews examined in this scoping review support the conclusion that personality traits have a robust association with tinnitus.

Some of the personality traits examined in this paper appear to share common underlying constructs. Neuroticism of the FFM and Stress Reaction as measured with the Multidimensional Personality Questionnaire (MPQ) both define the tendency to experience frequent, negative emotions. Extraversion and Social Closeness describe the tendency to exhibit sociability, emotional expressiveness and turning to others for comfort and excitement. The two key constituents of a Type D Personality are negative affectivity and social inhibition; again, showing overlap with characterizations of high Stress Reaction and low Social Closeness. Acceptance and Well-Being both reflect feeling good about self, and adapting a more open frame of mind.

The majority of personality traits outlined in this review appear to be potential moderators which, according to Andersson & Westin (53), can directly influence tinnitus distress. One possible mechanism by which personality traits can do so is explained by the Theory of Signal Detection model (166, 167). Personality traits can manipulate the response criterion placement when any given level of a signal becomes perceived as tinnitus. Individuals with increased awareness have the criterion placement more towards the left (will report even very low levels of the signal as tinnitus), whereas others require stronger signals to be present before reporting tinnitus. The Adaptation Level Theory (ALT) model of tinnitus highlights the interaction of tinnitus with the environment (5). The adaptation level (AL) acts as an internal reference point used to make sensory magnitude estimations of the tinnitus, and can
change over time (315, 322). A high AL leads to elevated and distressing tinnitus. One possibility is that ‘adaptive’ personality traits present in an individual facilitates AL shifts away from the tinnitus and supports habituation over time. In contrast, ‘maladaptive’ personality traits keep the AL for tinnitus elevated and prevent shifts away from it.

A multidisciplinary approach to tinnitus treatment is now common practice in clinic; however personality traits are not examined or addressed in much depth. It may be due to the belief that personality traits are not susceptible to change and thus, are not necessary for addressing from a tinnitus treatment perspective. It is understood that although relative positions of a person’s personality are stable over the life span, absolute levels of traits can be changed (46, 50, 167). Certainly, understanding the personality of the patient may help in the counselling process.

### 3.6.2. Affective Disorders

Among the questionnaire-based studies examined in this scoping review, 16 out of 21 studies found an association between depression symptoms and greater tinnitus distress. Of the five studies which found no association, two reported that depression/anxiety scores were elevated in relation to other measured psychological variables, but remained within the normal population range. Eleven of the 15 questionnaire studies concluded that higher levels of anxiety significantly correlated with higher tinnitus severity. The presence of depression or high tinnitus distress also led to greater difficulty in masking tinnitus using white noise. Individuals suffering from high depression or tinnitus distress may fixate their attention on the internal tinnitus sensations; thereby tinnitus may take on greater magnitude requiring more noise to mask. Prior literature reviews state that anxiety and depression are more common among tinnitus patients presenting in a clinical setting relative to non-tinnitus controls and can serve as good predictors of tinnitus distress. These reviews also acknowledge that tinnitus patients presenting at hospitals might be a subgroup of the larger general tinnitus population, with intensive symptoms.

Studies were predominantly cross-sectional in design using questionnaires; psychiatric diagnostics studies using systems as the DSM were limited. The advantages of having structured diagnoses are that more detailed information can be collected, it is reliable and greater predictive validity is present (369). On self-report scales, the presence of depressive
Symptoms can not only be due to a depressive disorder – but another psychiatric problem such as a personality disorder, dementia, addiction, bipolar disorder, etc. (369). Therefore it remains difficult to ascertain the directional relationship between affective disorders and tinnitus, and we cannot establish causality. There is hardly any evidence suggesting that the presence of affective disorders cause tinnitus itself-. It appears more likely that psychological characteristics affect how a person reacts to tinnitus, by amplifying symptoms and complaining. Stouffer & Tyler (406) measured pre-tinnitus onset depression at 11% and post-tinnitus onset at 39%. Statistical analysis was not however conducted on the data making it difficult to judge the findings’ strength. Individuals with higher anxiety levels during the first 4 weeks of tinnitus onset were more likely to develop distressing tinnitus (414). The large scale longitudinal study by Hebert et al. (405) across two years showed that tinnitus severity and prevalence varied significantly with changes in depression levels in the general population.

Moreover, distressing tinnitus symptoms can potentially “feedback” and affect the individual psychologically. Stobik et al. (404) found decompensated tinnitus patients (suffering significantly from tinnitus) were more susceptible to developing depression. Thus, regardless of which symptoms present first, it is possible that they can combine to form a vicious cycle and exacerbate each other. The other thing to consider is whether the existence of the condition is primary or secondary to the tinnitus. It is not clear whether tinnitus results in emotional problems such as anxiety and depression, or whether people with such problems are more likely to react negatively to the tinnitus. Among those diagnosed with a psychiatric disorder, higher rates of previous psychiatric disorders pre-tinnitus onset have also been observed among sufferers as well as higher rates of psychiatric illness in the family (391). Holgers et al. (421) reported that for 90% of tinnitus patients with anxiety or depression, the onset happened before or simultaneously with tinnitus onset.

The data examined in this scoping review predominantly applies to the help-seeking subgroup of tinnitus sufferers, as most were tinnitus patients presenting in ENT clinics. This group might show an increased association with psychological problems than in the general tinnitus population. The Krog et al. (417) study was conducted on a large scale general population sample where the association between anxiety, depression and tinnitus was not as strong. There was also no gradient, whereby symptom intensity correlated with anxiety and depression. Psychological differences are present between help-seekers and non-help-seekers,
such as help-seekers having greater psychological disturbances, higher Stress Reaction but lower tinnitus loudness than non-help-seekers (367, 398, 407, 429).

It is possible that the presence of certain mediating or third variables drive the expression of both personality traits/affective disorders and tinnitus. Langguth et al. (369) reviewed common neural pathways for both depression and tinnitus whereby hypothalamic-pituitary-adrenal (HPA) axis dysregulation and dorsal cochlear nucleus (DCN) hyperactivity can serve as underlying mechanisms for both conditions. The human gene variant for brain-derived neurotrophic factor (BDNF) has also been studied as a common susceptibility factor. Furthermore, higher levels of anxiety and depression were present not only among tinnitus patients, but also among other patients at the same clinic presenting with a variety of ENT problems (411). These effects remained even after controlling for various factors such as age, duration of condition, marital status, and occupation, presence of symptoms, change in symptoms and use of a hearing aid. The authors state that ENT health issues and tinnitus both have sensations and symptoms which are intrusive in nature and this creates anxiety and depression. Another key point is that there also may be symptom overlap between depression and the effects of distressing tinnitus. Nine out of the 13 most distressing disturbances/symptoms of tinnitus are also present in depression (369) (Figure 8). Certain symptoms of anxiety and depression also overlap. A considerable limitation of the findings may be that in studies where tinnitus severity and depression are both measured, the symptoms of both can be overestimated.

3.6.3. General Considerations

The personality trait and affective disorder studies that have been conducted to date are predominantly cross-sectional in design and questionnaire-based. The sample size used in these studies can also influence statistical power of findings. Three personality trait studies involved large scale population examination (21, 167, 375) of 172621, 3372 and 970 participants respectively. For affective disorders, the large scale population studies (21, 405, 417) involved 3372, 6215 and 51574 participants respectively. The majority of studies (29 studies) were conducted in Europe, 5 in UK, 12 in North America (Canada and USA), 1 in Australia, 1 in Israel, 1 in Brazil, 1 in Korea, 1 in New Zealand and 2 in Turkey. The mean age of participants in studies was approximately in the middle-age range (40-55). Participants of studies were predominantly tinnitus sufferers presenting in ENT clinics.
Control groups were only used in 9 of the personality trait and 11 of the affective disorder papers reviewed. These studies either compared tinnitus participants to 1) those without tinnitus, 2) those with hearing loss present and no tinnitus, 3) no hearing loss or tinnitus, or 4) normal hearing or a slight hearing loss. In instances where controls were recruited from the general population, measurement bias may arise (e.g. research volunteer bias). The duration of tinnitus in an individual can affect habituation and acceptance processes (181). The minimum duration of tinnitus was not specified in most studies; for those which did state criteria for tinnitus duration, it ranged from one month to having tinnitus at least one year. Persons with severe psychological disturbances such as schizophrenia, manic-depressive psychosis, dementia and behavioural disorders were excluded by 4 personality trait and 3 affective disorder studies. It is possible that the inclusion of these participants in these studies (or the exclusion of such participants in other studies) might have affected study findings, likely affecting trait composition or resulting in different rates of psychiatric diagnoses.
Another important consideration is the heterogeneity of measures used in studies for measuring personality, anxiety/depression and tinnitus loudness and/or distress, which can make comparisons between studies difficult. The most common measure of personality was the Eysenck Personality Inventory (EPI). The most prevalent psychological measurement scales were the Beck Depression Inventory (BDI), the Minnesota Multiphasic Personality Inventory (MMPI), the State-Trait Anxiety Inventory (STAI) and the Hospital Anxiety and Depression Scale (HADS) respectively.

3.6.4. Limitations of This Review

The scoping review is a relatively new methodology and is becoming increasingly popular for reviewing health research (430). The main aim of scoping reviews is to ‘map’ or summarize all the material available in this field without critically appraising the quality of individual studies (431). This is particularly useful when the topic is complex or has a heterogeneous nature, such as ours. However, it is acknowledged that the scoping review methodology has its own limitations. The quality of the data is not assessed and despite attempts to be comprehensive as possible, this review may not have identified all the relevant studies in the field. The search algorithm for this study included five different terms and 4 of the major health databases were searched. The use of other terms or databases may have yielded additional published scoping reviews. The articles were limited to those written in or translated to English. Another general issue which might have affected the studies selected is selective publication in scientific literature, mainly the tendency to publish positive results only. Mandatory reporting of findings is needed in order to correct this problem.

3.7. Conclusions

This scoping review was carried out to outline and summarize existing literature on personality traits and tinnitus and affective disorders (anxiety and depression) and tinnitus. Specific personality traits are found to have an association with tinnitus distress; these can be categorized under common terms – an individual with high tinnitus distress is also likely to display one or more of: high Neuroticism, low Extraversion, high Stress Reaction, higher Alienation, lower Social Closeness, lower Well-Being, lower Self Control, lower psychological Acceptance, have the presence of a Type D Personality and a more
externalized Locus of Control. It seems to be that personality traits drive tinnitus distress as a moderating variable, by influencing mechanisms of signal detection. This review also supports the notion that anxiety and depression are more prevalent among the tinnitus clinical population and at elevated levels. It is more difficult to judge the direction of this relationship. The similarities in symptoms of psychological disorders and tinnitus also make this difficult. It is acknowledged that the effects of other influencing variables such as age, gender, degree of hearing loss, etc. were not studied in this review.

Further research in this area could look at a controlled comparison of personality trait profiles of tinnitus sufferers and non-tinnitus individuals (by matching for other variables such as age, gender, degree of hearing loss, etc.) for the key traits identified in this review. Also, the existing literature has predominantly examined tinnitus loudness and distress associations with personality. It would be of interest to examine the relationship between key traits and various perceptual tinnitus characteristics such as pitch, location, or tinnitus changes to loud sounds. General future directions could be to examine how personality or psychiatric diagnosis impacts on tinnitus treatment expectations, treatment adherence and outcomes.
Chapter 4. The personality profile of tinnitus sufferers and a non-tinnitus control group
4.1. Preface

Publication

This chapter includes content from the article “The personality profile of tinnitus sufferers and a non-tinnitus control group” accepted for publication in The Journal of the American Academy of Audiology (in press).

What was undertaken?

A web-based survey measuring four key self-reported personality traits (social closeness, stress reaction, alienation and self-control) (66 items), tinnitus (60 items) and hearing handicap (10 items) was administered to 154 individuals with tinnitus and 61 age, gender and hearing level-matched non-tinnitus controls. Tinnitus sufferers displayed higher levels of stress reaction, lower social closeness, lower self-control and higher alienation than the control group. Alienation was related to tinnitus pitch and self-reported hyperacusis. Stress reaction correlated with self-reported hyperacusis, whether tinnitus sufferers had sought other treatments, and whether loud sounds made the tinnitus worse.

Why was this needed?

Current literature on personality and tinnitus is sparse because numerous personality traits have been examined and using different assessment tools. The majority of studies to date also did not employ appropriate comparison groups, which are necessary for various reasons, e.g. hearing loss itself can result in significant social and health problems, such as communication problems, loneliness, dependence and frustration. This study extracted four possible constituents of a core ‘tinnitus distress’ personality profile based on current research and allowed for a controlled comparison with non-tinnitus controls matched by age, gender and hearing level to see whether underlying profile differences exist, and also if personality traits levels correlated with various tinnitus characteristics assessed in typical clinical questionnaires (existing literature has predominantly examined tinnitus loudness and distress associations).

How did it contribute to the objectives of the PhD?

The four personality traits examined in this study differentiated tinnitus sufferers from non-tinnitus controls, and appear to be moderating variables which directly influence tinnitus
distress. The results also suggested that certain personality traits correlated with the clinical presentation of tinnitus. This study strengthened the role of personality traits as residual factors determining tinnitus magnitude under the ALT framework. High levels of stress reaction, low social closeness, low self-control and high alienation are conceptualized as ‘maladaptive’ residuals that result in elevated tinnitus perception and prevent habituation by diverting attention and auditory processing resources towards the tinnitus.
4.2. Abstract

**Objectives:** Four key self-reported personality traits (social closeness, stress reaction, alienation and self-control) were identified from previous research as being associated with tinnitus. These were compared between tinnitus and age-, gender-, and hearing level-matched non-tinnitus controls to see whether underlying profile differences exist, and if personality traits levels correlate with various tinnitus characteristics assessed in typical clinical questionnaires.

**Study Design:** A web-based personality survey was administered comprising of self-control, stress reaction, alienation and social closeness subscale questions of the Multidimensional Personality Questionnaire (MPQ) (48), The Hearing Handicap Inventory Screening Version (HHI-SV) (432), Tinnitus Functional Index (TFI) (110) and Tinnitus Case History Questionnaire (TCHQ) (122). 154 tinnitus (81 males, 73 females, mean age = 62.6 years) and 61 control (32 males, 29 females, mean age = 59.62 years) participants were recruited via email invitations to a tinnitus research clinic database, poster and social media website advertising.

**Results:** Tinnitus sufferers displayed higher levels of stress reaction, lower social closeness, lower self-control and higher alienation than the control group. Alienation was related to tinnitus pitch and self-reported hyperacusis measured using the tinnitus case history questionnaire. Stress reaction correlated with self-reported hyperacusis, whether tinnitus sufferers had sought other treatments, and whether loud sounds make the tinnitus worse.

**Conclusions:** The four personality traits examined in this study exhibited a consistent association with tinnitus perception and distress, and differentiated tinnitus sufferers from non-tinnitus control. Some of the traits also correlated significantly with certain characteristics measured in tinnitus history questionnaires. Personality traits are described in relation to ‘maladaptive’ residuals under the Adaptation Level Theory (ALT) model of tinnitus (5). The results of the study suggest that certain personality traits correlate with the clinical presentation of tinnitus.
4.3. Introduction

Subjective tinnitus is the involuntary perception of one or more sounds by an individual, in the absence of an external physical source (a phantom perception) (2, 34, 86). There is general consensus that tinnitus is essentially a central phenomenon, generated within the central nervous system with cortical and sub-cortical involvement (2, 34, 59, 76, 78, 127, 128), as a result of either some form of peripheral lesion or deafferentation (2, 3, 34, 129, 130) or alterations to top-down inhibitory mechanisms (8). Only a modest proportion (about 15–20%) of the population of patients with tinnitus experience disruption to quality of life and distress, such as disturbed sleep and concentration, problems with hearing, irritation and annoyance, anxiety and depression (11-13). The psychoacoustic characteristics of tinnitus alone do not fully account for tinnitus severity (used interchangeably with the term distress in this paper), or why some individuals are bothered by tinnitus while others are not (367). Likewise, the strength of the tinnitus signal itself (loudness) can predict distress, although it does not account for all tinnitus variability (330). Network tinnitus models based on functional neuroimaging evidence may account for this effect as discrepancies in activation patterns and altered neural connectivity between individuals with distressing and non-distressing tinnitus (79). Several auditory and non-auditory regions have been implicated in tinnitus distress, and correspond to consciousness, salience and emotional processing networks (4, 78, 79). These networks can differ depending on the underlying pathophysiology giving rise to tinnitus, and may also shape psychological responses to the tinnitus. Furthermore, De Ridder et al. (4) theorise that there are different tinnitus sub networks which represent clinical characteristics such as loudness, laterality, type (tone, hissing, etc.) alongside tinnitus distress. Large-scale integration is needed to bind together various anatomical and functional regions of brain activity to forming a unified conscious perception of tinnitus (4, 67). Resting state networks can change with time, with certain sub networks becoming more or less robust in activation (35).

An increasing body of literature suggests that certain personality traits often coexist with tinnitus; the presence of which may also contribute towards final tinnitus severity (5, 13, 20, 21, 53, 368, 369). Personality traits define the typical thoughts, actions, behaviours and interacting style of an individual (46-48). These dispositions are influenced by both genetics and the environment (49-52). Personality traits have been described as potential moderators of tinnitus distress (factors which have the potential to change an outcome directly), or in the
presence of a specific personality trait, tinnitus can become more distressing (interaction of the tinnitus signal and moderators to impact the final outcome) (53).

A scoping review of existing studies in this field conducted by Durai & Searchfield (433) concluded that an individual with high tinnitus distress is also likely to display one or more of the following traits (trait descriptions provided in Table 3): high Neuroticism (93, 374, 375, 391, 392), low Extraversion (93, 374), high Stress Reaction (93, 167, 367), lower Social Closeness, higher Alienation and lower Self Control (93, 167, 374, 377), lower psychological acceptance (378, 434), the presence of a Type D personality (93, 376) and a more externalized locus of control (180, 377, 397, 398). Differences in personality traits between those who do and do not experience tinnitus have also been observed. Among 32–year-old individuals, Welch & Dawes (167) observed those who perceived tinnitus had significantly lower Social Closeness, higher Stress Reaction, higher Alienation and lower Self Control than those who did not. However, this study did not match for age, gender and hearing level between tinnitus and non-tinnitus control groups, and was limited to a much younger age cohort than the age range in which tinnitus is most commonly observed (between 60’s and 70’s) (12). Also, tinnitus distress was measured with only a one-item question (“How annoying or upsetting is it [tinnitus]?” to which four replies were possible: not at all, slightly, moderately, and severe) (167). Greater levels of Neuroticism and lower Extraversion (93, 374), higher Alienation (167), lower Self Control (374) and Type D personality (93) have also been associated with tinnitus perception. From a neurophysiological point of view, the regions encoding certain personality traits in the cortex can become established as part of the tinnitus network; through which an increased number of neural connections, greater strength/synchronization and/or persistent co-activation between personality networks and tinnitus perception and/or distress networks can be elicited. However, the mechanisms which would drive this relationship are not comprehensively understood.

One possible explanation for manipulation of tinnitus perception is provided via the Theory of Signal Detection (166, 167, 435). This theory formulates the concept of a criterion which individuals, as active decision makers, use for separating incoming stimulus from random noise. The threshold level at which this criterion is placed can be along a distribution of signal strength (modelled as a Gaussian curve). Practical application for this theory are in examining participant response accuracy and the nature of errors within an experimental setting, and psychologists use the model to measure how decisions are made under conditions of uncertainty (435). High response bias would be interpreted as a low threshold criterion.
Table 3. Personality traits and trait descriptions in relation to tinnitus based on scoping review by Dural & Searchfield (452).

<table>
<thead>
<tr>
<th>Trait</th>
<th>Description</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroticism (FFM)</td>
<td>Tendency of an individual to experience negative emotions</td>
<td>Costa and McRae, 1992</td>
</tr>
<tr>
<td>Extraversion (FFM)</td>
<td>Tendency to exhibit sociability, assertiveness, emotional expressiveness and excitability</td>
<td>Costa and McRae, 1992</td>
</tr>
<tr>
<td>Agreeability (FFM)</td>
<td>Low competitiveness, low self-centeredness, and less susceptibility to anger</td>
<td>Costa and McRae, 1992</td>
</tr>
<tr>
<td>Stress Reaction</td>
<td>Tendency to experience frequent and intense negative emotions, including anxiety, distress, and anger; overacts to minor events</td>
<td>Tellegen, 1983</td>
</tr>
<tr>
<td>Social Closeness</td>
<td>Sociable, likes people, and turns to others for comfort</td>
<td>Tellegen, 1983</td>
</tr>
<tr>
<td>Self Control</td>
<td>Reflective, cautious, careful, rational; not impulsive</td>
<td>Tellegen, 1983</td>
</tr>
<tr>
<td>Alienation</td>
<td>Views the world in malevolent terms; expects mistreatment and betrayal; feels a victim of bad luck</td>
<td>Tellegen, 1983</td>
</tr>
<tr>
<td>Well-Being</td>
<td>Happy, cheerful disposition; feels good about self; and sees a bright future</td>
<td>Tellegen, 1983</td>
</tr>
<tr>
<td>Acceptance</td>
<td>More positive and open frame of mind, do not ruminate on past experiences and have a motivation to carry on with their life</td>
<td>Hayes et al, 1999</td>
</tr>
<tr>
<td>Anxiety Sensitivity</td>
<td>Tendency to fear anxiety related symptoms (bodily signs such as increased heart rate, sweating, muscle tension, headaches, etc.)</td>
<td>Taylor, 1995</td>
</tr>
<tr>
<td>Type D Personality</td>
<td>Greater tendency to experience negative emotions (negative affectivity) and are unlikely to express their emotions to others (social inhibition)</td>
<td>Pedersen and Denollet, 2003</td>
</tr>
<tr>
<td>--------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Locus of Control</td>
<td>External vs. internal, whether an individual believes that they are in control of their symptoms or not in control</td>
<td>Rotter, 1966</td>
</tr>
</tbody>
</table>

placement, with a highly probable chance of response occurring. This criterion is influenced by several determinants, and is able to change over time, following adaptation to the task, physiological state changes (such as fatigue) or the purpose or goal of the task. Welch & Dawes (167) hypothesized that personality traits may influence response criterion placement when any given level of a signal becomes perceived as tinnitus. Individuals with existing traits that increase awareness can have the criterion placement more towards a low signal detection threshold, whereas others require stronger signals to be present before reporting tinnitus perception (Figure 9).

**Figure 9.** The Gaussian curve represents the distribution of internal tinnitus signal strength. Personality traits may influence placement of an individual’s response criterion, which determines the threshold level at which the a tinnitus signal is separated from random internal noise and perceived. A) A low response bias correlates with a high threshold criterion placement, representing low awareness and a low probability of perceiving tinnitus. B) A high response bias correlates with the criterion set lower, with a higher probability of tinnitus perception. Adapted from (167), p. 688.
Searchfield et al. (5, 6) propose a similar reference point argument in the Adaptation Level Theory (ALT) model of tinnitus perception, which states that any magnitude estimate of tinnitus is not made in isolation but is dependent on the interaction between three components: the tinnitus signal, the presence of contextual or background sound and residuals (individual cognitive or behavioural factors). Personality traits are one of the residual components, alongside past experiences, prediction, emotion and physiological arousal), which is involved in computing an adaptation level (AL) for the tinnitus. This AL acts as an internal anchor/reference point used to make sensory magnitude estimations, and is susceptible to change over time and context (43, 315, 322). For loud tinnitus, a high internal AL is established – thus the tinnitus is perceived as being of high magnitude. One factor which precipitate this is when the tinnitus becomes a greater focus than real sound, and has high AL weighting given to it. In a similar manner, the distress experienced by tinnitus can also shift based on an internal reference point, potentially driven by non-auditory physiological mechanisms previously discussed. A high set-point for tinnitus AL can therefore characterize tinnitus which is not only louder but also one which can elicit greater negative emotions in an individual. The ALT model is advantageous as it accounts for how tinnitus magnitude and distress judgements can be altered by multiple, complex interactions including factors both inherent to the individual (such as personality) as well as alterable contextual factors (e.g. time of day, past experiences).

A limitation of existing personality studies has been the heterogeneity of traits examined and assessment tools used, meaning extraction and consolidation of data is difficult, e.g. search terms on academic search engines and medical databases. Despite the different terminology used, common key underlying constructs emerge within tinnitus distress-related traits, for example, the two main constituents of a type D personality are 1) negative affectivity, and 2) social inhibition: similar in definition to 1) high Neuroticism or high Stress Reaction, the tendency to experience frequent, negative emotions (48, 372), and 2) low Extraversion or low Social Closeness, the tendency to exhibit sociability, emotional expressiveness and turning to others for comfort and excitement (48, 372). Therefore it is possible to extract four key constituents of a core ‘tinnitus distress’ personality profile based on the definitions of each trait, these are: high Stress Reaction, high Alienation, low Social Closeness and low Self Control. Moreover, there was a lack of appropriate comparison groups in the majority of studies reviewed – only 9 out of the 25 studies examined by Durai & Searchfield (433) employed a control group. These studies either compared tinnitus participants to 1) those
without tinnitus, 2) those with hearing loss present and no tinnitus, 3) no hearing loss or tinnitus, or 4) normal hearing or a slight hearing loss.

This study aimed to empirically examine the core tinnitus distress personality profile by seeing if the four key traits of Stress Reaction, Alienation, Social Closeness and Self Control are significantly different between individuals with tinnitus and non-tinnitus individuals group-matched for age, gender, hearing aid wear, degree of hearing loss and degree of hearing handicap. The presence of significant differences will strengthen the hypothesis of personality traits as moderators of tinnitus. While tinnitus loudness and distress has been examined often, the relationship with other tinnitus characteristics such as pitch, location or tinnitus changes to loud sounds has seldom, if ever, been considered. Durai et al. (10) observed that tinnitus sufferers with high Social Closeness and high positive emotionality experienced an increase in perceived tinnitus loudness and distress under the presence of background noise. Individuals with low Stress Reaction and low negative emotionality showed higher objective tinnitus loudness matches under identical contextual noise settings. Theoretically, personality networks can also influence other tinnitus perceptual sub networks (related to pitch, location, tinnitus-external sound interactions, etc.) in an analogous manner to how they might interact with loudness and distress sub networks, however, the literature to date has examined predominantly tinnitus perception and distress. It was also of interest to examine whether these personality trait levels correlate with other tinnitus clinical presenting characteristics as assessed in typical history questionnaires. The results will be modelled and applied to the Adaptation Level Theory (ALT) model for tinnitus framework (5).

4.4. Methods

The methods used in this study were approved by the University of Auckland Human Participants Ethics Committee. A web-based survey (136 items for tinnitus participants; 76 items for non-tinnitus control participants) was administered via www.surveymonkey.com, an online survey development cloud-based service, to collect data for this study. Each participant answered the survey once, and the survey took approximately 20-25 minutes to complete.

4.4.1. Recruitment

A convenience sample approach (436) was adopted. In order to recruit participants for the tinnitus group, email invitations were sent out to all members on the University of Auckland
Tinnitus Research Volunteer Database (372 people from throughout New Zealand, majority from within Auckland). These are individuals with debilitating tinnitus who are interested in volunteering for tinnitus studies and clinical trials related to tinnitus relief. The link to the survey webpage was provided in the email invitation, and individuals who were interested could directly access and complete the survey. Participants for the control group were recruited through the University of Auckland Hearing and Tinnitus database (case history identified them to not have tinnitus currently), using poster (placed in the University of Auckland clinics and around campus) and social media website advertising, asking for people with hearing loss, in one or both ears, and without constant tinnitus (sounds heard in your ear such as ringing or humming when there is no external source actually creating the noise) to take part in the survey, again providing the link to the webpage if interested.

4.4.2. Participants

In total 157 tinnitus sufferers (42% response rate) and 66 control group participants responded to the survey. Respondents who did not answer more than 85% of the full survey were then excluded. Respondent who answered ‘None’ in response to the question regarding their degree of hearing loss were not included in the analysis (i.e. slight, mild, moderate, moderately severe, severe and profound were the categories of hearing loss used in the analysis of degree of hearing loss). For the final analysis 154 tinnitus (81 males, 73 females, mean age = 62.6 years, SD=8.99, age range=23-80) and 61 control (32 males, 29 females, mean age = 59.62 years, SD=12.51 years, age range =22-71) participants’ data were used. The mean raw TFI score of tinnitus participants was 87.63 (SD=22.53), and mean tinnitus duration was 18.12 years (SD=11.69 years, range =4-40).

4.4.3. Materials and Tests

The tinnitus group survey comprised of three sections: 1) Personality, 2) Hearing and 3) Tinnitus. The control group filled in the two sections of Personality and Hearing.

Age, gender and self-reported degree of hearing loss in both ears (slight, mild, moderate, moderately severe, severe or profound) was asked at the beginning of the survey for both tinnitus and control groups. The personality section had 66 questions in total taken from the Multidimensional Personality Questionnaire (MPQ) corresponding to subscales of Self Control,
Stress Reaction, Alienation and Social Closeness (48, 437). The full MPQ is a 278 item questionnaire, which has been extensively used as a personality measure and has high internal reliability and high validity (48, 373, 437). The MPQ was developed by Tellegen (48) through an exploratory approach to measure normal personality. It includes first-level personality traits that are also mapped onto higher-order super factors which define emotional and temperamental constructs of an individual, and together with trait information, can allow for high resolution of personality. Under the MPQ structure, the four personality traits under study map onto broader second-order factors of positive emotionality (Social Closeness), negative emotionality (Alienation and Stress Reaction) and constraint (Self Control). The response format was ‘True’ or ‘False’ or ‘Select A or B’ in response to self-description statements about personality.

Items are also included in the MPQ to assess validity of responses and to address whether participants have paid sufficient attention to item content: the Variability Response Inconsistency (VRIN) scale in which questions similar in content are presented, so non-matching answers (e.g. True for one question and False for the other) reflect inconsistent responses; the True Response Inconsistency (TRIN) in which questions opposing in content are presented, so matching answers (e.g. True for one question and also True for the other) reflect inconsistency; and the Unlikely Virtues (UNVIR) scale which contains 14-items indexing social desirability, that identifies respondents who are falsely likely to portray themselves in a socially acceptable manner.

**Hearing Section:** The 10-item Hearing Handicap Screening Version (HHI-SV) (432) comprised the second section, which measured the level of handicap to everyday life as a result of hearing loss as a score out of 40, and categorises impairment as follows: scores 0-8=no handicap, 10-24=mild-moderate handicap and 26-40=severe handicap. Only the raw HHI-SV score was used for analyses in this study.

**Tinnitus Section:** The final section incorporated the 25-item Tinnitus Functional Index (TFI) (110) which measures 8 important life domains of negative tinnitus impact: intrusiveness, sense of control, cognition, sleep, auditory, relaxation, quality of life and emotional. Again, the raw TFI score was used for analyses. The 35-item Tinnitus Case History Questionnaire (TCHQ) (122) asked participants to describe various characteristics of their tinnitus including location (left ear, right ear, both ears, inside the head, elsewhere), tinnitus onset (stress, change in
hearing, loud blast of sound, head trauma, other), pitch (low frequency, medium frequency, high frequency, very high frequency), whether it is constant or intermittent, whether their tinnitus changes in the presence of environmental sounds such as shower noise, water fall, music, etc. (participants answer yes, no or don’t know), number of treatments for tinnitus (none, one, several) or whether the participant experiences other related health problems such as chronic pain (yes, no), psychiatric problems (yes, no) or hyperacusis tendencies (discomfort and/or pain to loud sounds – participants answer always, often, sometimes, occasionally or never).

4.4.4. Statistical analysis

Statistical analysis was conducted using IBM SPSS ® Version 22 software. For all analysis, the level of significance was defined as 0.05. The specific statistical tests run for each analysis are reported in the Results section.

4.5. Results

The Shapiro-Wilk test for normality was not significant for all personality trait scores, both in the tinnitus group and control group. Levene’s Test for Equality of Variances was not significant for Self Control, Stress Reaction or Social Closeness. Levene’s test was significant for Alienation (p<0.001), and test results were adjusted accordingly for this violation of homogeneity of variance between tinnitus and control groups.

4.5.1. Demographics comparison by group

A demographic comparison of tinnitus and control groups by age, gender, hearing aid use and self-reported degree of hearing loss (ASHA, 2011) is provided in Table 4. Chi-squared analysis revealed no significant differences in the age, gender, wearing of current hearing aids or degree of hearing loss between the tinnitus and control groups (p > 0.05). Independent samples t-tests showed no significant difference in HHI-SV scores between the tinnitus (M=13.8, SE=1.3) and control (M=12.1, SE=0.80) groups. A One-way analysis of variance (ANOVA) conducted showed significant differences in average HHI-SV scores between the slight and mild,
moderate, moderately severe, severe and profound groups, between the mild and moderately-severe, and between mild and severe groups (F(5,166) = 18.438, p < 0.05) (Table 5). HHI-SV scores generally increased as degree of hearing loss progressed from slight to severe, then dropped for profound (Figure 10). There was no significant difference in TFI scores between the different degrees of hearing loss categories.

### 4.5.2. Correlations between personality scores, HHI-SV and TFI

Pearson correlations showed that among tinnitus sufferers, Stress Reaction scores significantly negatively correlated with Self Control (r = -0.365, p < 0.05) and Social Closeness (r = -0.296, p < 0.05) scores, and positively correlated with Alienation scores (r = 0.406, p < 0.05). Alienation and Social Closeness were significantly negatively correlated (r = -0.404, p < 0.05). HHI-SV scores were significantly positively correlated with Stress Reaction (r = 0.319, p < 0.05) and negatively correlated with Social Closeness (r = -0.296, p < 0.05). The total TFI score was significantly positively correlated with Stress Reaction (r = 0.296, p < 0.05) and with Alienation (r = 0.238, p < 0.05). Among the control group, Alienation was significantly positively correlated with Stress Reaction scores (r = 0.295, p < 0.05) and negatively correlated with Social Closeness (r = 0.162, p < 0.05). Stress Reaction and Social Closeness scores were significantly negatively correlated (r = -0.312, p < 0.05). HHI-SV scores for the control group were significantly positively associated to Stress Reaction scores (r = 0.196, p < 0.05), and significantly negatively associated with Social Closeness (r = -0.189, p < 0.05).

Table 4. Demographic comparison of tinnitus and control groups.

<table>
<thead>
<tr>
<th></th>
<th>% Tinnitus</th>
<th>% Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>55% (N=81)</td>
<td>54% (N=32)</td>
</tr>
<tr>
<td>Females</td>
<td>45% (N=73)</td>
<td>46% (N=29)</td>
</tr>
<tr>
<td>Age group</td>
<td>M=62.6, SD=8.99</td>
<td>M=59.62, SD=12.51</td>
</tr>
<tr>
<td>21-30</td>
<td>0.6% (N=1)</td>
<td>3% (N=2)</td>
</tr>
<tr>
<td>31-40</td>
<td>8% (N=13)</td>
<td>14% (N=9)</td>
</tr>
<tr>
<td>41-50</td>
<td>6% (N=10)</td>
<td>4% (N=3)</td>
</tr>
<tr>
<td>51-60</td>
<td>23% (N=36)</td>
<td>23% (N=13)</td>
</tr>
<tr>
<td>61 and above</td>
<td>62.5% (N=94)</td>
<td>56% (N=34)</td>
</tr>
</tbody>
</table>

Degree of hearing loss
<table>
<thead>
<tr>
<th>Hearing loss category</th>
<th>Slight (25% (N=39))</th>
<th>Mild (26% (N=40))</th>
<th>Moderate (29% (N=45))</th>
<th>Moderately severe (13% (N=20))</th>
<th>Severe (6% (N=8))</th>
<th>Profound (1% (N=2))</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>75% (N=116)</td>
<td>76% (N=47)</td>
<td>9% (N=14)</td>
<td>17% (N=24)</td>
<td>17% (N=11)</td>
<td></td>
</tr>
<tr>
<td>In one ear</td>
<td>9% (N=14)</td>
<td>8% (N=5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilaterally</td>
<td>17% (N=24)</td>
<td>17% (N=11)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HHI-SQ</td>
<td>35 (M=13.8, SD=4.01)</td>
<td>30 (M=12.1, SD=2.5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 5. Mean differences in HHI-SV scores between hearing loss categories. ‘*’, ‘**’ and ‘***’ indicate differences significant at the 0.05 level (2-tailed), 0.01 level (2-tailed) and 0.001 level (2-tailed) respectively.

### Mean differences in HHI-SV scores between hearing loss categories

<table>
<thead>
<tr>
<th></th>
<th>Slight</th>
<th>Mild</th>
<th>Moderate</th>
<th>Moderately Severe</th>
<th>Severe</th>
<th>Profound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slight</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>-6.20**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>-10.63***</td>
<td>-4.43</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderately Severe</td>
<td>-14.81***</td>
<td>-8.61***</td>
<td>-4.18</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>-17.21***</td>
<td>-11.01***</td>
<td>-6.58</td>
<td>-2.40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Profound</td>
<td>-12.21*</td>
<td>-6.01</td>
<td>-1.58</td>
<td>2.60</td>
<td>5.00</td>
<td></td>
</tr>
</tbody>
</table>
4.5.3. Personality Scores comparison by group and demographic characteristics

A mixed-measures ANOVA was conducted to compare personality scores for each of the four key traits with between-subject factor of group (tinnitus or controls) and within-subject factors of age, gender, hearing aid wear (left ear, right ear, both ears or none) and self-reported degree of hearing loss. Post-hoc Bonferroni tests were used to further compare significant main and interaction effects.

Significant main effects were present for each personality trait by group ($F(1,213)=6.997, p < 0.05$). The tinnitus group ($M=12.70, SD=4.15$) had statistically significant lower levels of Self Control than controls ($M=13.76, SD=3.26$) (Figure 11). The tinnitus group ($M=6.31, SD=4.17$) also displayed significantly greater Stress Reaction scores than controls ($M=4.59, SD=3.74$). Alienation scores were higher for tinnitus ($M=3.48, SD=3.87$) than control groups ($M=1.90, SD=2.26$), while Social Closeness scores were lower for tinnitus ($M=8.46, SD=3.57$) than controls ($M=10.11, SD=4.06$).

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**Figure 10.** Plot showing mean HHI-SV scores for each category of self-reported degree of hearing loss for all participants (tinnitus and controls).
Significant interaction effects were present between group and gender for Social Closeness (F(1,213)=4.112, p < 0.05), with the control group obtaining significantly higher scores for females (M=11, SD=3.86) than males (M=9.52, SD= 4). For Stress Reaction scores within each group, significant interactions were also observed between age and degree of hearing loss (F(13,167)=2.715, p < 0.05) (Figure 12). Among tinnitus respondents with slight hearing loss, the 41-50 age group (M=0.882, SE=3.471) had significantly lower Stress Reaction scores compared to the 51-60 group (M=8.167, SE=1.636), and 61 and above group (M=3.128, SE=0.753) had lower scores compared to 51-60 group. For mild hearing loss, the 31-40 group (M=7.5, SE=2.454) displayed higher scores than the 51-60 group (M=1.295, SE=1.341); while for moderate hearing losses the 31-40 group (M=9.333, SE=2.004) had higher scores than the 61 and above group (M=4.083, SE=1.129). For moderately severe hearing loss, a difference was observed with the 51-60 group (M=8, SE=1.735) having higher Stress Reaction scores than the 61 and above group (M=3.25, SE=1.272).
Within the control group, for slight hearing losses, significantly higher Stress Reaction scores were present between 31-40 age group (M=14, SE=3.471) when compared to the 51-60 group (M=4, SE=3.471) and the 61 and above group (M=6, SE=1.175). For the mild hearing loss category, 31-40 age group (M=0.53, SE=0.471) had significantly lower scores than the 51-60 group (M=8.667, SE=1.829). In the moderate hearing loss range, the 31-40 group (M=2.5, SE=2.454) had significantly lower scores than the 51-60 group (M=9, SE=2.126). Stress Reaction scores were significantly lower in the 31-40 age group (M=0.7105, SE=0.271) than the 51-60 group (M=8.5, SE=2.459) for controls with severe hearing loss.
4.5.4. Personality scores comparison by tinnitus characteristics

A repeated-measures ANOVA was conducted to compare each personality trait and tinnitus characteristics of: location (left ear, right ear, both ears, inside the head, elsewhere), tinnitus onset (stress, change in hearing, loud blast of sound, head trauma, other), pitch (low frequency, medium frequency, high frequency, very high frequency), whether it is constant or intermittent, whether their tinnitus changes in the presence of environmental sounds such as shower noise, water fall, music, etc. (participants answer yes, no or don’t know), number of treatments for tinnitus (none, one, several) or whether the participant experiences other related health problems such as chronic pain (yes, no), psychiatric problems (yes, no) or hyperacusis tendencies (discomfort and/or pain to loud sounds – participants answer always, often, sometimes, occasionally or never). Post-hoc Bonferroni tests were conducted to further analyze significant main effects.

A.
B.

Figure 12. Stress Reaction scores (A) Tinnitus group, (B) Control group) categorized by age of participants as well as degree of hearing loss. Significant differences are indicated by (*). Error bars represent +/- one standard error.

There were no significant differences in personality scores among tinnitus participants whose tinnitus was alterable by environmental sounds or non-alterable (or did not know). When examining other tinnitus variables, Alienation scores were found to be significantly related to tinnitus pitch \((F(3,147) = 3.581, p < 0.05)\). Post-hoc Bonferroni tests showed that high frequency tinnitus sufferers had higher Alienation scores \((M=2.20, SD=1.55)\) than medium frequency sufferers \((M=1.07, SD=0.854)\). Stress Reaction scores were significantly related to whether tinnitus sufferers had sought other treatments \((F(2,149) = 3.389, p < 0.05)\) and whether loud sounds make the tinnitus worse \((F(2,147) = 5.156, p < 0.05)\): with those seeking several treatments \((M=6.65, SD=3.66)\) having significantly higher Stress Reaction than those who had not had any treatments at all \((M=4.18, SD=3.58)\) and those whose tinnitus was made worse by loud sounds \((M=5.91, SD=3.57)\) having higher Stress Reaction than those whose tinnitus was not made worse \((M=3.84, SD=3.44)\). Also, Stress Reaction \((F(4,147) = 3.532, p < 0.05)\) and Alienation scores \((F(4,147) = 3.854, p < 0.05)\) and self-reported hyperacusis tendencies (discomfort and/or pain in the presence of loud sound) were significantly related. It was not possible to conduct post-hoc analyses on these because at least one group had
fewer than two cases. There were no significant differences in personality trait scores with regards to whether the tinnitus sufferer had chronic pain or not, onset, tinnitus location, constant or intermittent tinnitus or reported active treatment for any psychiatric problems.

### 4.6. Discussion

#### 4.6.1. Summary of Results

This survey experiment comparing underlying personality trait profiles found significantly lower Self Control, higher Stress Reaction, higher levels of Alienation and lower levels of Social Closeness in tinnitus sufferers compared to control participants with hearing loss and no tinnitus. Total tinnitus distress scores measured using TFI scores also significantly positively correlated with Stress Reaction and Alienation. This profile is consistent with that observed in previous studies regarding tinnitus perception and distress (93, 167, 367, 374). When personality trait levels were broken down by demographics, they did not largely vary by age, current hearing aid usage or degree of hearing loss for both tinnitus and control groups. There was an effect present for gender, with females in the control group demonstrating significantly higher Social Closeness than males. Males and females are thought to have general differences present for intrapersonal processes such as emotional processing and regulating conflict (438). It is also known that women more readily report their closeness in a relationship and their emotions more expressively than men (439). In both tinnitus and control groups, the level of reported hearing handicap was significantly positively correlated with Stress Reaction and negatively correlated with Social Closeness levels. However, the correlation was stronger for the tinnitus group. An interesting observation was that in both tinnitus and control groups, Stress Reaction appeared to increase naturally with age, with larger scores generally observed in the older age groups (51-60 and 61 and above) than for younger age groups (31-40 and 40-51). This was regardless of the presence or absence of tinnitus. Given that the age compositions of both groups were not significantly different, however, this age-effect would have been accounted for in this study.

Significant correlations were present within the traits examined. Broadly, traits which fell into the same super factor were positively correlated, and traits which fell into different super factors were negatively correlated: among tinnitus sufferers, Stress Reaction was significantly
negatively correlated with Self Control and Social Closeness, and positively correlated with Alienation. Alienation and Social Closeness were significantly negatively correlated. Among the control group, Alienation was significantly positively correlated with Stress Reaction scores and negatively correlated with Social Closeness. Stress Reaction and Social Closeness scores were significantly negatively correlated. This is consistent with the structure of the MPQ (48, 373). The primary traits represent fine-grain emotional and temperamental characteristics of an individual, which map onto broader super factors constructs that conceptualize the different dimensions of personality. Positive emotionality and negative emotionality super factors describe susceptibility to experience positive and negative emotional states respectively, and constraint describes tendencies of behavioural restraint versus impulsiveness. Therefore, it is possible for traits within the same super factor to be positively associated with one another, but inter- super factor correlations to remain negative.

With regards to interactions between personality traits and tinnitus perceptual characteristics, there was no reported association of trait levels with whether tinnitus was alterable by environmental sounds or not. This is contrast to Durai et al.’s (10) experimental findings where low Social Closeness and high Stress Reaction correlated with a decrease in perceived tinnitus loudness and distress with background noise. Also, no significant differences were present with regards to whether the tinnitus sufferer had chronic pain or not, the location of tinnitus, if the tinnitus was constant or intermittent or if the individual was currently under treatment for psychiatric problems. It is acknowledged that the wording in this question might be a bit ambiguous for interpretation, as a sufferer might still be affected by psychiatric problems but not be seeking active treatment for it. Salviati et al. (188) found that 48% of 114 patients in their study presented with psychiatric comorbidity, such as depression, somatization, obsession, and anxiety. Self-reported pitch in tinnitus questionnaires and Alienation were significantly related such that high frequency tinnitus sufferers displayed greater Alienation levels than medium frequency sufferers. Individuals who reported seeking several treatments for tinnitus had higher Stress Reaction than those who had not had any treatments at all. Likewise, elevated Stress Reaction was present among those whose tinnitus is made worse by loud sounds than those whose tinnitus did not change. Both Stress Reaction and Alienation levels significantly related to the tendency to experience hyperacusis. Stress Reaction and Alienation both fall under the negative emotionality super factor of the MPQ. De Ridder et al. (4) postulated that there are different and partially overlapping sub networks for tinnitus in the cortex, encoding various psychoacoustic characteristics such as loudness,
laterality, tinnitus quality (tone/hissing/noise), location, etc. These can interact and change over time to provide the final perception (4, 88, 440). It is possible that the presence of certain personality traits might be involved in specific sub network activation. There might be increased strength of neural connections coding ‘maladaptive’ personality traits with tinnitus loudness and distress, leading to persistent co-activation of these tinnitus networks, while the connections for ‘adaptive’ personality traits might not be as strong. However, this is a hypothesis and is in need of further investigation.

4.6.2. Study Limitations and Considerations

The study is correlational in nature; therefore, we cannot assess the directionality of relationships between personality traits and tinnitus, and we cannot establish causality. However, while it is possible for distressing tinnitus symptoms to potentially “feedback” and affect an individual psychologically (such as anxiety and depression) (433), it is not likely that the presence of tinnitus will give rise to personality trait dispositions. Secondly, given the multiple factors included in the mixed model analysis, it is acknowledged that it is possible to observe a significant effect by chance.

The inclusion of an appropriate control group is necessary for various reasons. Hearing loss itself can result in significant social and health problems, including: communication problems, loneliness, dependence and frustration (441, 442). Rutter and Stein (411) found higher anxiety and depression symptoms present among 124 tinnitus patients compared to 73 hearing loss patients without tinnitus. A drawback of this study arising from being a web-based survey was that objective measurements of hearing levels were not possible. Self-reported measures were used instead to assess the impact of hearing loss including self-reported degree of hearing loss, use of hearing aids, and hearing handicap scores, and this imposes limitations to the extent in which the findings can be applied to clinical settings in which hearing levels are measured using appropriate instruments.

The mild hearing loss group had significantly lower hearing handicap reported than the other groups. In general, there was increased hearing handicap as the level of hearing loss progressed between categories. The profound group HHI-SV score which comprised a small minority of participants (1% of tinnitus and 4% of controls) fell between the moderately-severe and severe group category. Upon analyses there were significant differences in hearing
handicap between groups, as measured by mean HHI-SV scores, however, the mean TFI scores did not significantly change across categories. Therefore, it can be concluded that this self-reported hearing loss measure differentiated between tinnitus-related and hearing-related handicap to an extent that is feasible for us to use self-reports for categorising degree of hearing loss.

The tinnitus group in this study predominantly consisted of participants 61 years or older (62.5%). Tinnitus occurrence and distress increases with age (11, 12). The highest prevalence rate for tinnitus is observable in the 60’s and 70’s age group, with subsequent decline in the older age groups (12). It is possible for tinnitus distress to be heightened for these age groups, potentially leading to higher mean distress levels. Personality questionnaires are a highly valid and stable way of measuring personality traits, and the measured traits can remain stable over several years (49, 443). A significant limitation of self-report questionnaires, especially concerning personality, however, is social desirability bias (444). This describes the tendency of an individual to untruthfully answer questions in order to be viewed favourably by others, or provide only responses which are socially acceptable. This typically involves over-reporting of socially favourable traits and under-reporting undesirable traits, and can seriously interfere with interpretation of average group trait composition measures. While the original MPQ attempts to minimise this bias using the 14-item index UNVIR scale, only 66 items were selected in this study and the full UNVIR scale was not used – therefore social desirability bias was not controlled for. By comparing levels between tinnitus and control groups, it is anticipated that any additional trait levels observed would correspond to a core tinnitus personality profile.

4.6.3. Modelling under the ALT framework & Clinical implications

Under the ALT model, an elevated internal AL is established for persistent tinnitus (5, 6). Therefore tinnitus is perceived as being of high magnitude and distress. It is postulated that high levels of Stress Reaction, low Social Closeness, low Self Control and high Alienation may act as ‘maladaptive’ personality residuals under this framework, which divert attention and auditory processing resources towards the tinnitus, thus increase its AL weighting. The theory of signal detection provides an example of how this might occur. The subsequent co-activation of various sub networks encoding tinnitus characteristics in the cortex with increased
awareness/salience might then potentially explain the relationship between personality trait and psychoacoustic tinnitus characteristics (4).

Although psychological interventions are widely applied, personality factors have not been given much consideration among current tinnitus treatment paradigms (20, 342, 368). Taking into account the contributory role of personality traits may open up treatment avenues for tinnitus. Within the context of obesity, for example, specific personality traits such as high Neuroticism and impulsiveness have been identified as risk factors (445). By identifying subgroups of patients with the relevant personality structure, the authors argue that at-risk individuals can be identified and specific treatment options such as psychoeducational or psychotherapeutic techniques may be personalised for these individuals. Similarly, the presence of specific personality traits when measured on a personality questionnaire may act as early markers for tinnitus susceptibility or severity over time, and can be used to target interventions at susceptible individuals. If an individual is able to gain an internal locus of control over their tinnitus through training (e.g. through instruction, reward/punishments or understanding the stimuli) (446), this might possibly shift the internal criterion for tinnitus detection over time. If this can occur, the effect of ‘maladaptive’ personality traits might be lessened (although not eliminated), and as a result it is possible for the AL weighting to also lessen for tinnitus with time. Further research would therefore be beneficial in this area.

Both genetic and environmental factors interact to create an individual’s personality (46, 52). Some of the personality traits identified in this study, such as Stress Reaction and Social Closeness, are difficult to change (167). If any change is possible, it will be gradual and dependent on the age of the individual – absolute level changes have been reported to be more pronounced during adolescence and the elderly years of life, due to biological maturation, social expectations and conditioning processes (47, 50, 372, 447). However, Costa & McRae (447) have acknowledged that due to study design, the findings from these studies may not apply to all cultures: for example, ethnic minorities and non-Western cultures might show different age trends.

4.7. Conclusions

Tinnitus sufferers in this web-based study displayed higher self-reported levels of Stress Reaction, lower Social Closeness, lower Self Control and higher Alienation than individuals
with hearing loss and without tinnitus; results were not confounded by the variables of age, gender and self-reported degree of hearing loss. These four constructs may reflect ‘maladaptive’ personality traits which divert attention and processing towards tinnitus and prevent habituation. This contributory effect of personality traits in tinnitus needs to be considered within clinical treatment settings, as the presence of these specific dispositions at higher levels can act as risk factors for identifying individuals who are prone to developing constant and/or debilitating tinnitus, or those who already have disruptive tinnitus and may benefit from psycho educational or psychotherapeutic interventions, locus of control training, etc. The extent and degree to which maladaptive traits, which are determined by both genetic and environmental factors, can be changed over time within the tinnitus population has not yet been investigated. How personality or psychiatric diagnosis impacts on tinnitus treatment expectations, treatment adherence and clinical intervention outcomes should be considered. Mechanisms by which the effect of maladaptive personality traits might be lessened include shifts to individual’s internal criterion for tinnitus detection over time and lowered adaptation level weighting of tinnitus.
Chapter 5. Examining the short term effects of emotion under an Adaptation Level Theory Model of Tinnitus Perception
5.1. Preface

Publication
This chapter includes content from the article “Examining the short term effects of emotion under an Adaptation Level Theory Model of Tinnitus Perception” submitted for publication in Hearing Research.

What was undertaken?
A behavioural experiment was conducted examining the effects of short-term emotional stimuli, differing along valence and arousal dimensions, on tinnitus loudness and annoyance. Stimuli were presented in two different modalities: auditory and visual. Six conditions consisting of a total of 120 items were presented in each modality. The duration of each item was 6 seconds with an inter-stimulus time of 6 seconds. Negative valence (unpleasant) auditory stimuli led to higher tinnitus loudness ratings in males and females and higher distress ratings in males only. Loudness matches of tinnitus remained unchanged. Visual emotional stimuli did not have an effect on tinnitus characteristics.

Why was this needed?
Current literature has predominantly focused on emotional affect as a resulting consequence of tinnitus. It remained difficult to discern whether emotion can modulate tinnitus perception and/or all emotions have an equal influence on tinnitus. Although underlying gender differences exist with regards to emotional regulation, it is not known if these gender effects translate across to tinnitus-related emotional changes. Furthermore, among non-tinnitus patients, the modality of emotional stimulus does not seem to affect general detection and processing networks in the brain. However, as tinnitus is an auditory phantom phenomenon, it is plausible that auditory emotional stimuli might affect tinnitus characteristics to a different degree than visual stimuli. All these gaps in current knowledge warranted further investigation.

How does it contribute to the objectives of the PhD?
An individual’s emotional state is one of the residual factors involved in computing an adaptation level (AL) for tinnitus under the ALT model. The results of this study supported the possibility for unpleasant auditory stimuli to prime or shape tinnitus perception and distress. Such stimuli increase the overall weighting given to the tinnitus component, and
tinnitus AL increases. Gender effects may also be present in the extent to which weighting shifts occur. These preliminary results were incorporated into the randomized clinical trial (Chapter 9) that investigated the effect of emotional associations in sound therapy, over a longer-term and outside of the laboratory environment.
5.2. Abstract

Objectives: Existing evidence suggests a strong relationship between tinnitus and emotion. The objective of this study was to examine the effects of short-term emotional changes along valence and arousal dimensions on tinnitus outcomes. Emotional stimuli were presented in two different modalities: auditory and visual. The authors hypothesized that (1) negative valence (unpleasant) stimuli and/or high arousal stimuli will lead to greater tinnitus loudness and distress than positive valence and/or low arousal stimuli, and (2) auditory emotional stimuli, which are in the same modality as the tinnitus, will exhibit a greater effect on tinnitus outcome measures than visual stimuli.

Study Design: Auditory and visual emotive stimuli were administered to 22 participants (12 females and 10 males) with chronic tinnitus, recruited via email invitations send out to the University of Auckland Tinnitus Research Volunteer Database. Emotional stimuli used were taken from the International Affective Digital Sounds- Version 2 (IADS-2) and the International Affective Picture System (IAPS) (448, 449). The Emotion Regulation Questionnaire (450) was administered alongside subjective ratings of tinnitus loudness and distress, and psychoacoustic sensation level matches to external sounds.

Results: Males had significantly different emotional regulation scores than females. Negative valence auditory stimuli led to higher tinnitus loudness ratings in males and females and higher distress ratings in males only; loudness matches of tinnitus remained unchanged. The visual stimuli did not have an effect on tinnitus ratings. The results are discussed relative to the Adaptation Level Theory Model of Tinnitus.

Conclusions: The results indicate that the negative valence dimension of emotion is associated with increased tinnitus magnitude judgements and gender effects may also be present, but only when the emotional stimulus is in the auditory modality. Sounds with emotional associations may be used for sound therapy for tinnitus relief; it is of interest to see if the emotional component of sound treatments can play a role in reversing the negative responses discussed in this paper.
5.3. Introduction

Tinnitus is the perception of sound in the absence of a sound source external to the listener (1, 3, 34, 125). Although the precise mechanisms are still not fully understood, tinnitus is thought to be generated within the central nervous system with cortical and sub-cortical involvement (2, 34, 59, 76, 78, 127, 128), potentially as a result of peripheral deafferentation (2, 3, 34, 129, 130) or alterations to top-down inhibitory mechanisms (8). Considerable disruption to quality of life and distress are experienced in about 15-20% of the tinnitus population, such as disturbed sleep and concentration, problems with hearing, irritation and annoyance, anxiety and depression (11-13). Tinnitus does not follow all the principles which normally apply to external sounds in relation to encoding, sensation and conscious processing, e.g. there is no related stored schema, does not follow typical energetic masking patterns, and does not generalize to other modalities (37-39, 343). Increasing evidence suggests that several auditory and non-auditory regions may be implicated in tinnitus distress, corresponding to consciousness, salience and emotional processing networks (4, 78, 79). These networks can differ depending on the underlying pathophysiology giving rise to tinnitus, and may also shape psychological responses to the tinnitus.

The Adaptation Level Theory (ALT) model of tinnitus (5, 6) is an ecological framework which takes a holistic approach to understanding the phenomenon and its complexity. This AL acts as an internal anchor/reference point used to make sensory magnitude estimations, and is susceptible to change over time and context (43, 315, 322). For loud tinnitus, a high internal AL is established – thus the tinnitus is perceived as being of high magnitude. In a similar manner, the distress experienced by tinnitus can also shift based on an internal reference point, potentially driven by non-auditory physiological mechanisms (88, 180, 330, 331). A high set-point for tinnitus AL can therefore characterize tinnitus which is not only louder but also one which can elicit greater negative emotions in an individual. The final AL magnitude estimates of tinnitus, as well as distress judgements, are derived by multifaceted interactions between the following: the focal component (tinnitus), contextual component (any background noise or applied sounds), and residual components (individual cognitive and behavioural characteristics, such as past experiences, prediction, emotion, personality traits, and physiological arousal) (5, 6, 10). There is also influence from the environment, both the immediate surroundings (e.g. physical surroundings, time of day) and broader factors, including their culture, beliefs, work, relationships, moral support and social environment.
Attention and auditory scene analysis processes are weighting factors, which help determine which component is given predominance at any time.

An individual’s emotional state is one of the residual factors involved in computing an adaptation level (AL) for tinnitus. Emotion defines a specific, affective reaction to a particular event, and is typically of shorter duration than a mood (54). Models of emotion suggest that there are two key dimensions of emotion: valence (relating to the level of pleasantness/lack of aversiveness and describing emotional states varying on a continuum from positive to negative feelings) and arousal (relating to level of physiological arousal, and describing emotional states on a continuum between calm and excited) (451), although the two dimensions are not orthogonal (449, 452). Components of arousal and valence together may conceptualize stress as an emotional state (451). Processing of emotion involves the limbic system in the brain: predominantly the amygdala, hippocampus and insula (55). Extensive neural interactions are present between the amygdala, hippocampus and auditory system for interpreting emotional sound (56).

Both the amygdala (453) and auditory cortex (454) are activated more in response to unpleasant sounds when compared to neutral sounds, and electrophysiological studies have shown faster response times to negative than positive stimuli (455, 456). Irwin (457) observed that in young adults with normal hearing, sounds which evoked a pleasant or unpleasant emotional response engaged different neural networks including the right amygdala, compared to neutral sounds. Sounds which differed in arousal level did not have a significant effect. A neurophysiological model of emotional coding proposed by Kumar et al. (132) based on dynamic causal modelling techniques (for inferring effective connectivity) suggests that aversive/unpleasant stimuli are first processed and decoded in the auditory cortex before being relayed to the amygdala for emotional interpretation. The acoustic features of emotional stimuli modulated connectivity from the auditory cortex to the amygdala, while reciprocal connections were modulated by the level of unpleasantness of the stimulus (132, 133). Omigie et al. (133) extended on this model and showed connectivity from the amygdala to auditory cortices was modulated by general emotional content - including pleasant stimuli and musical stimuli, although research has predominantly examined negative stimuli in relation to the amygdala This may form the underlying neural basis by which emotional content of sounds influence saliency and processing of auditory object representation within the auditory cortex.
Gender differences in neural activity relating to emotional regulation have been observed (458). McRae et al. (458) suggest that women may use positive valence (pleasant) emotions more in reappraising negative emotions than men; men may also rely less on cognitive emotional regulation strategies and use more automatic emotion regulation than women, as evidenced by decreased prefrontal, amygdala, and ventral strial region activation. Individual differences in emotional response to external stimuli are considered to arise in part from use/lack of use of emotional regulation strategies (450), particularly regular use of emotional reappraisal (controlling attention to and/or cognitively changing meaning of emotionally evocative stimuli) and emotional suppression (purposefully inhibiting emotional response or behaviour to stimuli from naturally occurring). These determine which behaviour or emotional states are exhibited, inhibited or altered within a given context, and may be driven by social expectations and norms (459). Age can also influence emotional processing (460).

Using fMRI, Mather et al. (460) observed that older adults (70-90 years old) had a reduced level of change in amygdala activity for unpleasant images compared to young adults (18-29 years old). However, increased amygdala activity levels were observed for pleasant images when compared to the young group. It is proposed that aging may result in a redistribution of cognitive functioning in relation to emotional stimulus processing.

Alterations to the limbic system are one of the most commonly studied neurophysiological mechanisms in chronic tinnitus (3, 8, 57, 59, 78). In tinnitus network models, emotion networks form part of the functional networks which are differentially activated between those with distressing and non-distressing tinnitus (4, 9, 78, 83). Various resting state fMRI models show increased resting state connectivity between the auditory cortex and amygdala in tinnitus patients (314) as well as between the parahippocampus and insula and the auditory cortex (57, 313, 461). Significant changes in limbic system activity are present among individuals with tinnitus and normal hearing (when compared to healthy controls) (462). In a task-based fMRI study by Carpenter-Thompson et al. (463), participants were required to respond as soon as possible if the auditory stimuli played to them were pleasant, unpleasant or neutral. Participants with tinnitus and no hearing loss, and participants with tinnitus and hearing loss demonstrated faster response times to affective sounds than those with hearing loss and no tinnitus. Pleasant sounds resulted in greater activation of the bilateral hippocampus and right insula in tinnitus patients compared to those without hearing loss or tinnitus. Compared to those with no tinnitus but hearing loss, the left parahippocampus was activated more in tinnitus patients. Golm et al. (464) observed increased activity in the insula
and frontal regions in individuals with tinnitus compared to non-tinnitus controls while viewing unpleasant sentences vs. neutral sentences. There were no significant differences in parahippocampal response between the two groups. Unpleasant sounds mimicking the tinnitus have been found to activate the tinnitus network more strongly than neutral tones (152). Similarly, simulation of tinnitus (using an aversive tinnitus-like auditory stimuli) in patients without tinnitus was found to lead to the activation of comparable neural networks including the limbic system (453, 465).

Jastreboff’s (59) neurophysiological model of tinnitus suggests that the co-activation of negative emotions associated with the tinnitus signal at its onset can result in classical conditioning over time; with the negative reinforcement forming a feedback loop potentially giving rise to increased tinnitus signal detection and distress. Raushecker et al. (8) have taken this connection further and suggested that there might be a causal role of emotion in tinnitus. According to Raushecker et al. (8), the limbic system normally acts as a noise-cancellation mechanism at the level of the thalamus and prevents the tinnitus signal (unpleasant, unwanted noise) from reaching the auditory cortex and conscious perception. However, if the limbic system is compromised, the tinnitus signal is relayed to higher centres triggering the cortical changes, giving rise to chronic tinnitus. However, this model is not congruent with current neuroimaging models for how information transfer occurs within the cortex, which suggest sound is already decoded in the auditory cortex before being sent to the limbic system. Empirical exploration of this theory is needed.

The ALT model proposes that emotion can act as a residual which influences tinnitus perception and/or distress by altering the reference point which is used to make tinnitus magnitude judgments. Therefore, it is possible for emotional states to prime or shape perception and response to tinnitus via top-down, higher order influences even if there are no changes to bottom-up processing of incoming neural signals. This is in line with findings from a recent cross-sectional study by Probst et al. (330) examining data from 658 respondents tracking their tinnitus characteristics on a smartphone application. It was observed that self-reported everyday emotional states modulated the relationship between tinnitus loudness and the resulting tinnitus distress experienced. Arousal mediated the loudness-distress relationship over long periods of time, while holding valence constant but this effect disappeared after controlling for valence and stress. However, valence was a mediator of the tinnitus loudness-distress relationship even after controlling for arousal and stress.
Current literature has predominantly focused on emotional affect as a resulting consequence of tinnitus and changes in functional connectivity between emotional and auditory processing neural regions. It remains difficult to discern whether emotion can modulate tinnitus perception, as theorized under the ALT model, and if so, whether all dimensions of emotion (and all levels of valence and arousal) will have an equal influence on tinnitus. Although underlying gender differences exist in common literature with regards to emotional regulation, it is also not known if these effects translate across to tinnitus-related emotional processing changes.

It was the intent of this study to examine if emotional priming will result in short-term changes in behavioural measures of tinnitus characteristics: loudness level matches and subjective ratings of tinnitus loudness and annoyance. Given that negative emotions and stress form aspects of tinnitus distress, and the complex altered auditory-limbic system functional connectivity which has been observed with tinnitus, it is hypothesized that negative valence stimuli will induce greater tinnitus loudness and annoyance than positive valence stimuli, and that high arousal stimuli will induce greater loudness and annoyance than low arousal stimuli. It was of interest to administer emotional stimuli in two modalities – visual and auditory. Among non-tinnitus patients, the modality of emotional stimulus does not seem to affect general detection networks in the brain and identical networks have been activated for processing of visual stimuli as well as auditory stimuli (313). Given the complex nature of tinnitus (as an auditory phantom phenomenon), it is plausible that auditory emotional stimuli might affect tinnitus characteristics to a different degree than visual stimuli. Emotional stimuli, which are in the same modality as the tinnitus, are hypothesized to have a greater effect on tinnitus outcome measures than visual stimuli. The results will be modelled and applied to the Adaptation Level Theory (ALT) tinnitus framework.

5.4. Methods

The methods were approved by the University of Auckland Human Participants Ethics Committee.

5.4.1. Recruitment
Email invitations were sent out to 60 members randomly selected from the University of Auckland Tinnitus Research Volunteer Database (372 people from throughout New Zealand, majority from within Auckland). These are individuals with debilitating tinnitus who are interested in volunteering for tinnitus studies and clinical trials related to tinnitus relief. The inclusion criteria were: participants needed to be aged over 18, have constant tinnitus, sufficient vision (corrected vision accepted) to see images on a standard LCD computer monitor screen 1.5m away, hearing in the normal to a moderate-severe loss range, and normal middle ear function.

5.4.2. Participants

Twelve females (mean age = 51.73, SD = 20.36) and 10 males (mean age = 65.63, SD = 10.49) took part in the study.

5.4.3. Materials and Tests

**Experimental Stimuli**: Auditory stimuli were taken from the 120-item International Affective Digital Sounds Version 2 (IADS-2) (449). Visual stimuli came from the 120-item International Affective Picture System (IAPS) (448). The IADS-2 and IAPS have been developed to provide a set of normative material for experimental investigations into emotion. The stimuli differ in ratings of valence (level of pleasure that is related to a given affective state, ranging from positive to negative) and arousal (intensity of a given affective state ranging from energized, excited, and alert to calm, drowsy, or peaceful). Twenty items were selected from each of IADS-2 and IAPS to be assigned into each experimental condition. Paired samples t-tests showed that the set of stimuli selected for each experimental condition differed significantly from each other in terms of mean ratings and standard deviation (Table 6). While participants were seated in a sound-treated booth (ISO 8253-1), auditory stimuli were presented bilaterally via speakers positioned 1.5 m on each side of the participant at 45°, with loudness set at a comfortable listening level. The duration of each auditory item was 6 seconds with an inter-stimulus time of 6 seconds. A break of 5 minutes was provided between each condition. Images were presented on a computer screen positioned about 1.5m in front of the participant, with appropriate image resolution. Each picture was presented for 6 seconds with an inter-stimulus time of 6 seconds. The 10-item
Emotion Regulation Questionnaire (ERQ) (450) was also administered to all participants before the experiment. This assessed individual differences in regular use of two strategies for emotion regulation or control: emotional reappraisal (controlling attention to and/or cognitively changing meaning of emotionally evocative stimuli) and emotional suppression (purposefully inhibiting emotional response or behaviour to stimuli from naturally occurring) using self-statement ratings. It was of interest to determine whether participants significantly differed their underlying response to emotional stimuli.

**Study Design:** Participants attended two sessions spaced two weeks apart. During the first session, participants were divided into two groups to receive either stimulation first: auditory or visual. Pure tone audiometry and tympanometry was conducted to ensure participants matched inclusion criteria. A two-channel Grason Stadler GSI-61 audiometer was used. Measurements were undertaken using Telephonics TDH-50P supra-aural (0.25 – 8 kHz) and high frequency circumaural Sennheiser HDA-200 headphones (9 – 16 kHz). Tinnitus testing was carried out on custom tinnitus software (® The University of Auckland) using HDA-200 headphones. Tinnitus pitch match was assessed throughout the test frequency range of 0.25 – 16 kHz using a two-alternative forced-choice (2AFC) method. Each tone was presented at a sensation level of 15 dB SL. Pitch match was then compared to tones one octave above and below to rule out octave confusion. The measurement was repeated until two repeatable responses were obtained. Sensation level matching was obtained using the pitch-matched stimulus sound at 30 dB above the threshold level and decreasing it slowly in 2 dB steps until the participant stated it was same loudness as their tinnitus. This was repeated three times, and the average of the last two runs was taken. This was subtracted from the threshold level, to obtain a level match in dB Sensation Level (dB SL). Minimum masking level (MML, in dB SL) was obtained using a NBN stimulus, raising it from the threshold level until the participant reported that the tinnitus was no longer audible. This procedure was repeated three times, and the average level was calculated. This was subtracted from the threshold level to give the MML match in dB SL.

Each group were then exposed to 6 different experimental conditions in their assigned modality: Positive valence, Neutral valence, Negative valence, High arousal, Neutral arousal, Low arousal. The conditions were counter-balanced in order. At the end of each condition, participants rated the set of experimental stimuli on a 10-point scale for valence ranging from
Table 6. Differences in mean ratings of valence and arousal between study experimental conditions.

<table>
<thead>
<tr>
<th>AUDITORY</th>
<th>Mean Ratings</th>
<th>Standard Deviation</th>
<th>Significance (two-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Valence – Negative Valence</td>
<td>5.446</td>
<td>0.127</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Positive Valence – Neutral Valence</td>
<td>2.562</td>
<td>0.082</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Neutral Valence – Negative Valence</td>
<td>2.884</td>
<td>0.151</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Arousal Highest - Arousal Lowest</td>
<td>3.238</td>
<td>0.272</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Arousal Highest - Arousal Neutral</td>
<td>1.239</td>
<td>0.166</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Arousal Neutral - Arousal Lowest</td>
<td>1.999</td>
<td>0.251</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>VISUAL</th>
<th>Mean Ratings</th>
<th>Standard Deviation</th>
<th>Significance (two-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Valence – Negative Valence</td>
<td>4.826</td>
<td>0.106</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Positive Valence – Neutral Valence</td>
<td>2.088</td>
<td>0.386</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Neutral Valence – Negative Valence</td>
<td>2.738</td>
<td>0.502</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Arousal Highest - Arousal Lowest</td>
<td>3.03</td>
<td>0.120</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Arousal Highest - Arousal Neutral</td>
<td>1.239</td>
<td>0.166</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Arousal Neutral - Arousal Lowest</td>
<td>1.537</td>
<td>0.117</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

1 (set of stimuli are highly negative and unpleasant) to 10 (set of stimuli are highly positive and pleasant) and on a 10-point scale for arousal ranging from 1 (set of stimuli are calm and peaceful) to 10 (set of stimuli are highly energizing and exciting). Participants rated their subjective tinnitus loudness and distress using 10-point rating scales ranging from 1 (tinnitus is not audible at all/ tinnitus is not annoying/distressing at all) to 10 (tinnitus is very loud/tinnitus is very annoying/distressing). A Loudness Level Match was also obtained. In the second session, participants were exposed to the same conditions but in the other
modality (e.g. first session: Auditory, second session: Visual). The same participant responses were obtained.

5.4.4. Statistical Analysis

Independent samples t-tests were used to compare scores between males and female in the emotional regulation questionnaire. A mixed measures ANOVA was used to compare tinnitus outcome measures across experimental conditions (within-subject factor) and between genders (between-subject factor) for both auditory and visual stimuli. Post-hoc Bonferroni tests were used to further compare significant main and interaction effects.

5.5. Results

Males (M=30.1, SD=3.31) had significantly higher emotional reappraisal scores than females (M=21.9, SD=5.87; t=3.55, p < 0.05). Males (M=16.5, SD=3.85) also had significantly higher emotional suppression scores than females (M=12.8, SD=2.31; t=2602; p < 0.05). Studies of norms for the ERQ (450) also report significant differences in emotional suppression, with males displaying higher suppression than females, and this is partly associated with social norms and role expectations.

When examined as a group, there were no significant changes in tinnitus loudness ratings, annoyance ratings and loudness level matches across the auditory or visual experimental conditions. In response to the auditory stimuli, females demonstrated a significant difference in loudness ratings between the experimental conditions (F(5,19)=2.397, p < 0.05) (Figure 13). The tinnitus loudness ratings for the Positive Valence condition (M=5.0455, SD =1.69) were significantly lower than the Neutral Valence condition (M=5.7273, SD =1.62), and lower than the Negative Valence condition (M=6.5, SD =1.82). Although the mean tinnitus loudness ratings decreased as levels of arousal were decreased across conditions, these changes were not statistically significant. Similar to females, males showed a significant difference between experimental conditions (F(5,19)=3.257, p < 0.05). Males had lower tinnitus loudness ratings for the Positive Valence condition (M=3.00, SD =0.94281) than the Neutral Valence condition (M=4.1, SD =1.20) and Negative Valence conditions (M=4.8, SD =1.81). There were no significant differences across the arousal conditions. In general, it was observed that loudness ratings were lowest for the Arousal Neutral condition in males, and
highest for the Arousal Highest condition. The Arousal Lowest condition was very similar (M = 5.2, SD = 1.54) to the Arousal Highest condition (M = 5.3, SD = 1.50). Both females and males did not show significant differences across the visual experimental conditions. However, the items used for the negative valence condition in the experiment also had significantly greater mean arousal levels than for the neutral valence condition (p < 0.05) and positive valence condition (p < 0.05).

For annoyance ratings, females did not show significant differences in either the auditory or visual conditions. Males had significant changes in tinnitus annoyance ratings across auditory experimental conditions (F(5,19)= 2.878, p < 0.05) (Figure 14). Tinnitus annoyance ratings for the Neutral Valence condition (M = 4.1, SD = 0.526) were significantly lower than the Negative Valence condition (M = 5.2, SD = 0.623; p < 0.05).

There were no significant differences in tinnitus loudness level matches for males and females in response to either visual or auditory experimental conditions.

A.
B.

**Figure 13.** Mean tinnitus loudness ratings for (A) females and (B) males across experimental conditions. Significant differences are indicated by (*). Error bars represent +/- one standard error.

**Figure 14.** Mean tinnitus annoyance ratings across experimental conditions. Significant differences are indicated by (*). Error bars represent +/- one standard error.

### 5.6. Discussion

In this study males had significantly higher emotional reappraisal and higher emotional suppression than females, indicating that they were more likely to reinterpret situations to
reduce the severity of negative responses or to exchange a negative attitude for a more positive attitude and more likely to suppress negative emotions respectively (450). This finding is consistent with the general variability present between women and men in emotional regulation and the subjective experience of emotion (466, 467). Particularly, neural activity in the orbitofrontal cortex, the anterior cingulate cortex, the insula and the amygdala are different between the two groups suggesting informational processing differences (468).

Females and males had the lowest tinnitus loudness ratings for auditory stimuli with positive valence, followed respectively by auditory stimuli neutral and negative in valence. The differences between the conditions were significant. For both females and males, changes in levels of arousal were statistically insignificant between conditions. However, it was also noted that items in the negative valence condition in this experiment also had significantly greater arousal rating levels than for the neutral valence condition and positive valence condition. Tinnitus loudness level matches did not change across conditions. The time delay between ending the stimulus set and starting the loudness level match was never more than a minute for participants, however, it is noted as a possibility that the effects of priming might have reduced during this time delay. The results of this study indicate that priming with emotional stimuli in the short-term can modulate subjective tinnitus perception and tinnitus distress. Under the ALT, residual components such as emotion can hypothetically affect tinnitus perceptual judgments by increasing or decreasing the level of weighting which is placed on the tinnitus, hence increasing the tinnitus AL (5, 6). Based on the results, we postulate that stimuli with negative valence (i.e. are generally unpleasant) increase weighting towards the tinnitus focal component, leading to increased magnitude judgements and perceived tinnitus audibility. Literature on emotional priming commonly reports enhanced learning of and memory for information that is congruent with an individual’s mood (469, 470). Bower (469) proposes an associative network model of memory storage where semantic network of represented concepts or schematas exist. Emotional state is one of the many informational nodes which make up a schema (471, 472). The mood of an individual can influence how easily assessable a specific schema (the “mood-congruent” schema) is from memory storage and this schema is more likely to be used for interpreting incoming information and make related judgments. One possibility is that within higher-order processing, for tinnitus schemata to be congruent with negative valence emotion, such that negative valence stimuli prime activation of tinnitus perception and distress-related memory
networks, such that it is increased in cognitive weighting and more attention is paid towards it.

The findings from this study complement previous findings that emotion affects general auditory and cognitive processing among tinnitus sufferers, such as that found by Carpenter-Thompson et al (463). Using a web-based task, Andersson et al. (412) have also observed that in tinnitus patients, the brain preferentially allocated processing to emotionally salient words related to tinnitus (an emotional Stroop effect), e.g. ‘peep’ and ‘tone’. This effect has been found in a number of emotional disorders, such as generalized anxiety disorder, social phobia and eating disorders (473), however the precise mechanisms underlying this effect are not yet fully understood. Ooms et al. (474) found that severely distressed tinnitus patients processed threatening affective information (fearful or angry) much faster than non-threatening stimuli (happy), similarly to how highly anxious individuals processed affective information. Variations in mood or emotional states affected impulse noise-induced tinnitus onset among young military people psychologically normal and with normal hearing (475). This might imply that emotion also affects vulnerability of the auditory system to stress.

Among non-tinnitus patients, the modality of emotional stimulus does not seem to affect general detection networks in the brain and identical networks have been activated for processing of visual stimuli as well as auditory stimuli (313). Tinnitus as an auditory phantom percept however appears to be distinctly driven by auditory emotional stimulus. This is despite resting state functional connectivity networks of tinnitus also including areas of the visual cortices (occipital cortices) (313, 476, 477).

Most models of tinnitus agree that there is an underlying tinnitus signal, but that an activation of several other regions is involved in the conscious detection and judgement of the tinnitus (4, 59, 123). These judgment processes are prone to influence from emotional and other higher-order sources as discussed previously. The objective match, which is made when an external test stimulus is introduced and the individual has to match it with an internal AL, can remain unchanged if the underlying tinnitus signal strength remains unchanged. But the perceptual interpretation of tinnitus can be altered, as in this case.

Interestingly, valence was the dimension of emotion most responsible for weighting shifts. This is in line with the Probst et al. (330) findings, which found valence to mediate the relationship between reported tinnitus loudness and distress within day-to-day life. Arousal did not appear to do so exclusively; however, the items used for the negative valence
condition also had greater levels of arousal present indicating that arousal might have an influencing effect to some degree, although not a direct effect. Models of emotion generally agree that there is some overlap between the two dimensional constructs (448, 449, 452). Steinmetz et al. (478) postulate the role of arousal in activating the emotional memory network in the brain among individuals is dependent on the valence level of the information to be remembered. For negative affective stimuli, levels of arousal increased amygdala connection strengths to other regions such as the inferior frontal gyrus and middle occipital gyrus, whereas for positive stimuli, arousal showed decreased connection strengths. The fact that processing of arousal is at least partly dependent on stimuli valence might explain the lack of effect seen when examining the dimension of arousal alone (assuming valence levels are similar for the three levels of arousal).

Gender differences were present for tinnitus distress and interaction with emotion. Men had significant changes in tinnitus annoyance ratings across auditory experimental conditions, being lower for the Neutral Valence condition than the Negative Valence condition. However, females did not show any significant changes. When interpreted under the ALT model, we can speculate that for men, negative valence stimuli might place higher weighting on tinnitus for both loudness and distress perceptual judgements, whereas for females, negative valence drives higher weighting for tinnitus loudness judgements only. Past studies suggest that tinnitus is experienced differently between the two genders. While the severity of tinnitus intensity is similar between men and women (107) or higher in men correlated with greater levels of occupational noise exposure and hearing loss, and less use of noise protection (11, 94, 479), women generally tend to experience greater tinnitus distress than men and are more likely to report tinnitus (34, 94, 167, 366). The greatest differences between male and females distress levels is among older patients (≥60 years of age) (479).

This difference has been attributed to differences in coping with stress, differences in habituation and vulnerability to long-term stress (167) and differences in prefrontal cortex activity (58). Sex differences are also present in other health conditions, such as chronic pain (480) and migraines and headaches (481). Changes to emotional processing can occur as a result of aging itself, due to peripheral deafferentation, neuroplastic changes, etc. which may result in a redistribution of cognitive functioning in relation to emotional stimulus processing (460). This can be a confound as tinnitus prevalence increases with age (12). The mean age of male participants was also greater on average than female participante; it was not possible to filter out the influence of age in this study.
5.7. Conclusions

In this investigation of the relationship between short-term emotion and tinnitus outcomes, it was found that negative emotions elicited by negative valence stimuli and presented in the auditory domain led to higher subjective tinnitus loudness ratings in males and females. Higher subjective distress ratings were also present in males only, following presentation of negative valence (unpleasant) auditory stimuli. Negative valence stimuli are proposed to increase the weighting placed on tinnitus adaptation level under the ALT model of tinnitus. One possible way in which this can occur is by negative valence emotional priming which makes tinnitus perception and distress-related memory schemas more easily accessible and more likely to be used for interpreting incoming information. Visual stimuli did not have an effect on tinnitus. Males and females in this study demonstrated significant differences in emotional regulation as well as in the relationship between emotional affect and tinnitus.

It should be stressed that the results are preliminary and further research is needed in this area. Specifically, long-term emotional change effects need to be considered and outside of the laboratory environment. Future directions could examine whether emotional regulation or meta-cognitive training can benefit tinnitus patients, or examine whether current treatments such as mindfulness training affect emotional information processing. Sounds with emotional associations can be used for sound therapy; it would be interesting to see if the emotional component of sound treatments can play a role in reversing the negative responses discussed in this paper.
Chapter 6. A review of auditory prediction and its potential role in tinnitus perception
6.1. Preface

Publication

This chapter includes content from the article “A review of auditory prediction and its potential role in tinnitus perception” submitted for publication in the Journal of the American Academy of Audiology.

What was undertaken?

A narrative review of existing literature relating to predictive processing within the auditory system, and predictive coding, auditory memory and tinnitus. The review concluded that the Bayesian brain hypothesis may underlie how auditory prediction and sequential processing of auditory objects may occur. Electrophysiological measures of auditory prediction error commonly involve the mismatch negativity (MMN) paradigm. Tinnitus can be initially processed as an auditory object, and theoretical arguments exist for the notion of continuous prediction errors influencing driving tinnitus perception and distress.

Why was this needed?

To a certain extent, tinnitus may be processed in a similar manner to external sound by the hearing system; however, this processing appears to be interrupted at the later stages of analysis. It is not fully understood what creates this disruption. Tinnitus sufferers also display general global disruptions of attention and working memory. The auditory system regularly predicts future auditory events based on patterns in incoming sound. A new hypothesis is that missing input reaching the cortex generates continuous prediction errors, which alongside signal salience and lack of existing memory representations, may interfere with normal auditory analysis and generate tinnitus perception. Processing of these prediction errors utilizes cognitive and attentional processes; the reduction in remaining cognitive reserve may therefore explain impaired performance on conscious attention and memory tasks. Integrating current published information specifically in relation to tinnitus, prediction and auditory memory can allow for better understanding of the nature and extent of prediction and memory influences on tinnitus.

How does it contribute to the objectives of the PhD?
Prediction is a residual factor under the ALT model, and the prediction error hypothesis is compatible with the ALT; it can provide an explanation regarding underlying mechanisms by which prediction as a residual may exert influence on tinnitus magnitude. Constant prediction errors generated due to missing auditory input will theoretically divert attention towards residual and tinnitus components, and subsequently increase tinnitus AL weighting. However, there are scant published empirical studies which have directly tested this hypothesis. Also, most of the electrophysiological studies of prediction used the MMN under the oddball paradigm. This may pose limitations as it is debatable whether the MMN represents prediction error or auditory adaptation. Another drawback is that the oddball paradigm does not appropriately model more complex auditory phenomenon. It was of significance that prediction and prediction errors be examined further in order to obtain greater understanding and fill in gaps in current knowledge. These issues were addressed by conducting an electrophysiological study using stimuli with greater levels of variation discussed in Chapter 8. The ALT model predicts that sound therapy which varies in the level of predictability will have different effects of tinnitus. This is explored in the behavioural experiment and feasibility trial discussed in Chapter 7 as well as in the randomized clinical trial discussed in Chapter 9.
6.2. Abstract

**Objectives:** To obtain a comprehensive narrative synthesis of current research in relation to auditory prediction and its potential role in tinnitus perception and severity.

**Study Design:** Green et al.’s (2006) narrative review methodological framework was followed. The key words: Prediction Auditory, Memory Prediction Auditory, Tinnitus AND Memory, Tinnitus AND Prediction in Article Title, Abstract, and Keywords were extensively searched on four databases: PubMed, Scopus, SpringerLink and PsychInfo. All study types were selected from 2000-Current (End of 2016). Reference lists of articles were reviewed to identify any further relevant studies. Articles were short listed based on title relevance. After reading the abstracts, and applying exclusion criteria, the remaining studies were chosen for charting data.

**Results and Conclusions:** The hierarchical predictive coding model based on the Bayesian brain hypothesis attentional modulation and top-down feedback serves as the fundamental framework in current literature for how auditory prediction may occur. Predictions are integral to speech and music processing, as well as in sequential processing and identification of auditory objects during auditory streaming. Although deviant responses are observable from middle latency time ranges, the mismatch negativity (MMN) waveform is the most commonly studied electrophysiological index of auditory irregularity detection. However, limitations may apply when interpreting findings due to the debatable origin of the MMN and its restricted ability to model real-life, more complex auditory phenomenon. Cortical oscillatory band activity may act as neurophysiological substrates for auditory prediction. Tinnitus has been modelled as an auditory object which may demonstrate incomplete processing during auditory scene analysis (ASA) (Searchfield et al, 2012; Searchfield, 2014) resulting in tinnitus salience and therefore difficulty in habituation. There are theoretical proposals for a relationship between prediction error and tinnitus, but few published empirical studies. Studies of oscillatory band changes in tinnitus show contradictory findings.
6.3. Introduction

Tinnitus is the perception of sound in the absence of sound in the environment (1-4). The precise mechanisms giving rise to tinnitus perception and distress are still not fully known, although it is now understood to be generated as a result of peripheral lesions in the auditory system. This results in altered input to the cortex triggering cortical neuroplasticity changes (including neuronal hyperactivity, synchronized neural activity, cortical map changes and memory retrieval) which ultimately gives rise to the perception of tinnitus (2, 9). It is important to note that tinnitus is not a disease in itself, but a presenting symptom in various underlying diseases and pathologies (29, 73, 75, 205, 482). If a cause is discernible, it is most likely to be noise-induced hearing loss. Some 15-20% of the tinnitus population experience disruption to quality of life (11, 12), manifesting as impaired concentration, problems with hearing, irritation and annoyance, anxiety, depression, disruption of everyday activities and disturbed sleep (11, 13, 87). The complexity of influences on tinnitus also extends to influences from an individual’s culture, beliefs, work and social environments (6). Self-perceived tinnitus magnitude (a combination of loudness, severity and tinnitus awareness) has been hypothesized to be the result of interplay between spontaneous and driven auditory activity, personality, emotion, attention and memory (5, 6, 10).

To a certain extent, tinnitus may be processed in a similar manner to external sound by the hearing system, undergoing feature extraction, schema formation and auditory object formation (5, 6). The auditory cortex (AC) carries out significantly complex processing (483). Top-down feedback connections exist from the AC to all levels through the auditory pathway, in addition to several multisensory projections. Prediction of future auditory events also occurs within this framework (484, 485). The evolutionary advantage of prediction is to reduce environmental uncertainty and ensure that sensory processing is economical (64, 65) and regularities or patterns in incoming sound allows the system to identify objects in complex auditory scenes (61). Both temporal (concerning ‘when’ or onset of a stimulus) and formal regularities (‘what’ or physical features of stimulus) can be used to determine future events (486, 487). Moreover, first-order formal regularities can be established (e.g. frequent repetition of a tone) as well as more complex, higher-order formal regularities (e.g. semantics of speech, music) (62). The formation of higher-order formal regularities appears to be automatic to a certain extent and dependent on the repetition probability of events (488). For external sound input, recent studies suggest that auditory prediction does not occur
independently within unimodal sensory areas, but also integrates input from other regions such as the visual and motor systems (489).

A new proposition is that dysfunctional prediction processing may also give rise to the phenomenon of tinnitus. According to De Ridder et al. (7, 67), deafferentation at the peripheral auditory level results in missing input reaching the cortex for certain frequencies which generates a topographically-restricted prediction error. Subsequent attentional diversion alongside central plasticity processes may ultimately give rise to the sensation of tinnitus. Such prediction errors are also consistent with models of tinnitus that suggest an important role for auditory scene analysis in tinnitus (61, 68-70), and can help explain tinnitus saliency and bridge the gap between peripheral lesions and central compensatory processes. The nature of literature in relation to predictive coding system in the auditory system is extensive; current knowledge is spread over several domains of psychoacoustics, neuroimaging/electrophysiology and neuroscience, higher semantic speech and music, and multisensory networks to name a few. To assess the feasibility of the prediction error hypothesis in tinnitus generation and perception, it is of interest to obtain comprehensive narrative syntheses of published information specifically in relation to tinnitus, prediction and auditory memory.

Better understanding of the nature and extent of auditory prediction and memory influences on tinnitus can significantly contribute to the current literature regarding underlying mechanisms, which currently does not focus on these factors.

6.4. Methods

Green et al.’s (490) narrative review methodological framework was selected for conducting this literature overview. This style is advantageous in presenting a broad perspective on the topic, bridging between scattered assortments of articles and enabling for conclusions to be drawn based on the scope of current findings. The key words: Prediction Auditory, Memory Prediction Auditory, Tinnitus AND Memory, Tinnitus AND Prediction in Article Title, Abstract, and Keywords were extensively searched on four databases: PubMed, Scopus, SpringerLink and PsychInfo. All study types were selected from 2000-Current (2016). Reference lists of articles were reviewed to identify any further relevant studies. Articles
were short listed based on title relevance. After reading the abstracts, and applying the exclusion criteria (minimum age of participants less than 18, involving human subjects only, article not available in English or topic irrelevant to study purpose), the remaining studies were chosen for charting data. The inclusion of papers was made by consensus between co-authors in order to provide information regarding predictive and/or memory processes directly related to tinnitus. The literature was then organized thematically, according to common idea threads.

6.5. Results and Discussion

6.5.1. Bayesian prediction processes and neural prediction error coding in the auditory system

The Bayesian predictive coding model is a fundamental framework in existing literature and all relevant studies into auditory prediction appear to hold this as basic premise (491, 492). The Bayesian brain hypothesis states that in situations of uncertainty, the brain relies on internal probabilistic models to optimize function (155). Incoming sensory input is combined with existing prior knowledge to generate predictions. At each level of the sensory processing hierarchy only the prediction error, the difference between incoming sensory input and existing internal memory representation (involving both short-term memory storage as well as long-term representations), is passed onto the next level for processing. Redundant acoustic signals are canceled at multiple levels (inferior colliculus, thalamus, and cortex) (493). The novelty of unpredictable sounds is given higher priority by the brain and allocated greater resources for processing. Based on this latest sensory input, internal memory representations are also updated and these changes are passed via top-down projections to alter receptive field properties of low-level sensory units for future events.

The neural mechanisms for auditory prediction error coding are still not comprehensively understood. Wacongne at al. (494) propose that differences between spiking excitatory thalamic input and spiking inhibitory predictive input can code violations, via inhibitory interneurons. Top-down feedback signals then re-adjust predictions via synaptic plasticity learning for future events. Ramaswami et al. (493) similarly suggest that familiar signals are cancelled out by the presence of inhibitory (mirror) images which are neural memory representations of past sounds. Low-level sensory neurons have been observed to behave in a
similar dynamic fashion to a perceptual Bayesian brain system: when two sensory neurons have overlapping input, the neuron which can provide an interpretation/explanation for the input will laterally inhibit the other from responding to the same input (Lochmann et al., 2011). Rubin et al. (495) used computational modelling to examine an oddball sequence of two tones with varying probabilities. For the majority of primary auditory cortex neurons, trial-by-trial response fluctuations were present correlating with the level of prediction error present, sometimes accounting for more than 50% of response variability. The memory representations had unexpectedly long durations (lasting for 10 or more stimuli) but were coarse, low-level representations, moreover, predictive power was inversely related to the complexity of the information recently presented. It is possible for neural models of mechanisms proposed to co-exist.

6.5.2. Evidence for auditory predictive processing

Experimental studies directly assessing auditory prediction have been conducted. Nazimek et al. (496) found differential brain activity between expected and unexpected sounds, with the later evoking greater left temporal and insula activation. Precision of prediction error processing significantly correlated with neural activity levels in specialized auditory sensory areas used for making perceptual decisions in a study by Hesselmann et al. (497). Prediction-related activity and actual stimulus responses showed significantly overlapping and indistinguishable sources in the left superior temporal gyrus (498). The activation of the neural representation of a stimulus when a stimulus is predicted closely resembles memory retrieval processes (499). In instances of redundant predictions, Pieszek et al. (500) observed that both predictions were processed by the system and compared against the other - when one of the regularities was violated, there was an additive error signal present representing the sum of the two prediction error signals. The degree of temporal prediction irregularities simultaneously present affected response times in a short-term memory scanning task; this effect was independent of the set size effect (501).

The vast majority of evidence comes from the literature examining complex, higher-order auditory predictive processing in speech and music recognition. Comprehension of speech in everyday life often relies on the ability to ‘fill in gaps’ of missing information, using context or prior speech. Reduced AC processing is present in circumstances where top-down feedback from frontal regions and/or speech production regions can accurately pass down
predictions regarding speech signals (483). The active hypothesis-and-test model proposed by Skipper et al. (483) states that predictions about incoming speech sounds are generated by speech production (posterior ventral frontal) regions of the brain using existing neural templates from past speech. The role of the AC is to confirm or deny these predictions – this ‘neural reuse’ of speech production regions leads to more economical processing. In the absence of predictions, the AC processes the sounds completely. Lyu et al. (502) observed violations in spoken language comprehension expectations to elicit stronger activations of the left anterior superior temporal gyrus and the ventral inferior frontal gyrus (IFG), with top-down feedback from the left ventral IFG to the anterior temporal regions potentially generating predictions. When speech is degraded, both intrinsic (e.g. the context of the speech) and extrinsic (e.g. other modality aids such as visual cues, accompanying facial movement) provide predictive cues for comprehension. Meaningful speech resulted in less auditor cortical activation compared to less meaningful sounds (483). The level of intrinsic prediction cues provided in the intelligibility of sentences significantly correlated with ability to behaviourally extract linguistic information (503). Leonard et al. (504) conducted a study using direct cortical recordings. The left frontal cortex had preceding increased neural activity (thought to be the generation of predictions in language areas), followed by increased activity in the bilateral auditory cortex in real-time with the missing speech.

Music perception involves the collaboration of simple level predictions such as melody, beat and harmony, overlaid by complex formal regularities that operate based on higher-order schema (505). Ohmae & Tanaka (506) suggest that depending on rhythm speed, the brain may use either temporal grouping of discrete sounds or longer-term temporal prediction of upcoming stimuli to detect stimuli absence. Regions of the inferior frontolateral cortex which is involved in attention orientation (507-509), ventrolateral prefrontal cortex (507, 510) and superior temporal gyrus (507, 508) play a role by implication in musical prediction and musical violation processing.

6.5.3. Prediction in auditory scene analysis

Auditory scene analysis (ASA) describes the process by which our auditory system analyses incoming sounds and separates it into distinct streams and auditory objects (e.g. water running, speech, a car horn) (61, 68-70). Both the ‘what’ and ‘where’ characteristics of
sounds need to be identified, requiring complex integration of semantic, spatial processing, memory and attention. Winkler & Schröger (492) outline in their review and theoretical framework how auditory scene analysis and auditory deviance detection often utilize common predictive inferences, following Bayesian principles.

Detecting regularities or patterns in incoming sound allows the system to identify objects in complex auditory scenes (60, 61). In experimental studies where two concurrent tones were administered and participants were asked to selectively attend to one tone, the presence of temporal regularities in the distractor tone enabled for easier stream segregation than if the distractor tone was irregular in nature (511, 512). If two tone sequences had temporal regularities present, there was also increased probability of hearing two sound streams (513-515). New auditory input may be delivered as a sensory event representation to the next level of processing; this representation not only encodes sensory features but also specifies how this sound is related to the current auditory context and current goals of the individual (492). Unitary sensory memory representations are then created and used form predictions and create auditory objects (492, 516). Sequential grouping cues may utilize Gestalt principles such as the old-plus-new heuristic (69) whereby the auditory system removes continuations of previous sounds from incoming stimuli before proceeding to analyze novel input (61, 517). Units of regularities stored in auditory short-term memory may be a percept, such as spatial location or pitch (518). Mill et al. (519) suggest that the auditory system constantly switches between various alternative chains before assigning the incoming sound to a final auditory object. As in other predictive processes, attention can have a strong modulating effect on the formation of auditory regularities (61, 493). Novel auditory objects are flagged as salient as a result of higher levels of attention diverted towards them (493).

**6.5.4. Electrophysiological evidence related to auditory predictive processing**

Event-related potentials (ERPs) can act as indicators of predictive processes, spanning over large time frames and arising from either low-level regularity detection or by top-down feedback for anticipatory future events (for reviews, see (61, 280)). The mismatch negativity (MMN) marker is most prevalently used to detect auditory deviances (260, 282, 500). This is typically elicited 100–200 ms in the frontocentral regions after onset of random deviant
auditory input in an auditory oddball paradigm. Other deviance responses in literature include the N1 (or N100, often observed 75-130 ms after stimulus onset (310)) and P3 response (P3b or P300, observed between 300-900 ms after stimulus onset, contingent on attention and localised over frontal, parietal and medial temporal regions (284, 285)); P3a can also be elicited before 300ms due to novel stimuli (305).

Reduced MMN amplitudes have been found for patterned sequences compared to random sequences (520). Todd and Mullens (521) observed smaller MMN amplitudes for deviants preceding a previous deviant than for random deviants. Todd et al. (522) demonstrated the MMN amplitude to be proportional to the probability of a deviant occurring and this effect was robust over multiple temporal scales. Lecaignard et al. (523) also observed a decrease in MMN response to predictable deviants within a sound sequence altering only in temporal predictability. When language-specific phonological rules were violated in speech input, Ylinen et al. (524) observed increased MMN amplitudes and the presence of P3a waveforms. Bendixen et al. (525) observed a larger MMN response for spoken sentences with omitted speech segments where the final speech segment had been predictable, compared to unpredictable. Strauss et al. (526) concluded based on the absence of P3 and incomplete structure of the MMN in sleep compared to wakefulness that both short-term and longer-term auditory predictive coding maybe disrupted during sleep. Based on findings regarding time scale, brain topographies and modulation by attention, the MMN may reflect predictive error processing while the P3 might involve attention orientation towards deviant stimuli (63) and updating of neural memory representations for future events (283, 527). Deviations to regular temporal structure resulted in enhanced N1 responses (63), while higher stimulus probability based on timing resulted in significant N1 suppression (528). Reduction in N1 responses were found for familiar melodies compared to unfamiliar melodies, regardless of octave-transposition (529).

Detection of auditory regularity violations within oddball paradigms can also be observed at much earlier latency ranges than that corresponding to the MMN, particularly with the middle latency response (MLR) (530-533) that occur within 10-60ms after stimulus onset in the auditory cortices (267). Bendixen et al. (64) found that ERPS generated within the first 50ms after the expected onset of a fully predictable tone are identical to that elicited upon presentation of the actual tone. These may detect low-level simple irregularities (but not to
more complex violations and may not generate predictions), supporting the hierarchical
nature of auditory predictive processing. Early modulations may also detect the most salient
source of acoustic information, and aid in auditory streaming (61, 69, 517). Cornella et al.
(534) found that changing perceived location but not stimulus repetition in a complex tone
paradigm led to changes in MLR responses. Stimulus location change and repetition both
resulted in MMN changes. Leung et al. (535) found that only frequency deviants led to
enhanced MLR responses; frequency, duration, intensity and interaural time difference
deviants all generated significant MMNs. Cornella et al. (536) found that for chirps delivered
in either a predictable or random location or omitted, an attenuation in MLR was only present
for regular chirps compared to random chips. In the late latency response range, both changes
in predictability and omissions led to significant differences in cortical responses.

There has been considerable debate whether the MMN origin reflects prediction signal error
or is the result of neural adaptation (274, 281, 537-540) (Figure 15). Gain adaptation of
neurons responding to the repeated stimuli in the oddball paradigm can cause habituation of
the volume over time. The deviant stimulus induces activation of less suppressed cells
therefore relatively greater amplitude is recorded as an ERP response. In order to separate out
the deviant responses evoked by changing a feature of the stimulus form that due to
prediction error exclusively, Symonds et al. (541) developed a unique tone-sequence stimulus
in which only temporal expectations were violated (the time duration of each sequence)
without altering any stimulus parameters. The expectation violation response differed in
timing, scalp distribution (specific left-lateralized frontal MMN) and the extent of modulation
from attention from the traditional MMN response. The authors suggest that the MMN
response may be formed from multiple overlapping processes and is not exclusively
reflective of prediction error. Therefore, there is some limitation to the extent to which
findings using MMN can be applied. Another disadvantage is that the repetitive long string of
tonal stimuli played is less representative of complex real-world auditory phenomenon (61,
517, 538). Bendixen (542) used noise to degrade the quality of tone sequences and measured
cortical responses; the covering of a predictable tone was not significantly different to the
covering of an unpredictable tone. The specific stimuli and paradigm used in testing
predictive processing therefore seems to have a considerable effect on results.
Figure 15. Schematic representations of the memory-based and adaptation model of the MMN. Top: In the memory-based model, a stimulus is analysed by an N1-generating transient-detector system and a separate, MMN-generating system that first analyses the stimulus for its features (frequency, intensity, duration, etc.). The result is deposited in sensory memory. A comparison process compares the features of incoming stimuli with representations of past stimuli in the sensory memory store, and, when the two differ, an MMN response is generated. Also shown is the beginning of a stimulus sequence, four standards (S) followed by a deviant (D), and the event-related responses produced by the separate N1 and MMN generators to the stimuli. The N1 is largest for the first standard. In contrast, the MMN generator reacts only when the deviant follows an already established memory.
trace for the standards (red curve). Therefore, it produces no response to any of the standards, including the first stimulus in the sequence. Bottom: In the adaptation model, the standards and deviants activate overlapping neural populations. The repetitive standard leads to cells tuned to the standard to become adapted. When the deviant is presented, non-adapted cells — “fresh afferents” — contribute to an enhanced response. Being in a non-adapted state, the MMN generator responds vigorously to the first standard of the sequence. It also produces attenuated responses to the subsequent standards. In this model, the N1 and MMN are generated by the same neural populations, and the MMN is, essentially, an enhanced N1 response. Reproduced with permission from (274), p. 68.

6.5.5. Role of attention in prediction

Regularity formation and deviation detection can act independently of attention (543, 544). Attention (broadly referring to the ability or power to concentrate mentally (128, 332) appears to serve the purpose of enhancing rather than generating predictive processes. Chennu et al. (545) observed using EEG and MEG that attention modulates the strength and precision of prediction errors generated for omissions. Auksztulewicz and Friston (546) used MEG to show that MMN deviance responses were enhanced by attention; this was linked to an increased gain of inhibitory interneurons. Hsu et al. (547) observed enhanced N1 waveforms for consciously attended versus unattended stimuli. The greatest N1 amplitude was observed in the attended condition for predictable stimuli, compared to random stimuli. Attention and intention of the listener may modulate signal detection and the gain of the prediction error signal sent to higher-order levels of processing (297, 548).

6.5.6. Role of oscillatory bands in auditory prediction

Rhythmic or repetitive neural activities are present within the cortex, termed neural oscillations (100, 144). These are labelled according to bands of frequency oscillations as follows: delta (approximately 1–4 Hz), theta (approximately 4–8 Hz), alpha (approximately 8–13 Hz) and gamma (approximately 30–60 Hz) (100, 144). Various brain functions are realized by simultaneous oscillations or coupling between different bands (148). If there is a decrease in sensory input needing to be processed, oscillatory patterns may change to slower rhythms, indicating that cellular firing rates and oscillations may be coupled at the thalamocortical level (67). The Thalamocortical Dysrhythmia (TCD) theory (149, 150) states
that sensory deafferentation triggers a cascade of events whereby spontaneous resting state alpha rhythms subsequently move to theta band rhythms, and persistent theta, gamma and delta activity is established within localized brain regions (7, 67, 78, 549, 550). Oscillatory bands may serve as a neurophysiological substrate for temporal prediction, which can increase neural sensitivity (increase signal-to-noise ratio) of predictable, task-relevant input (551). Morillon & Schroeder (551) illustrate this using the example of speech processing which involves integration of delta, theta, and low-gamma oscillations for prediction. Arnal et al. (552) propose that gamma bands transfer prediction errors to higher-order regions while top-down feedback information is nested on beta bands. The level of gamma activity in the cortex should therefore increase proportionally to prediction error. Fujioka et al. (553) measured an increase in beta wave amplitudes over time to always reach a maximum just prior to the introduction of the next sound in the sequence. Chang et al. (554) observed beta fluctuations in the auditory cortex to be modulated by frequency deviances. Dürschmid et al. (555) conducted a study using subdural electrocorticographic electrodes and demonstrated that longer-term global irregularities correlated with frontal gamma activity; short-term irregularities correlated with temporal cortex activation. Sedley et al. (556) also conducted an experiment using electrocorticography in three patients having neurosurgical treatment for epilepsy. A stream of complex tones was presented which were perceived as being random, although the pitch changes followed specific rules. Prediction errors were found to be explained partly by changes in local gamma band oscillations; the accuracy of predictions were related to alpha band levels; changes to predictions were related to beta oscillations.

6.5.7. Tinnitus as an auditory object in ASA

The Adaptation Level Theory (ALT) model of tinnitus views tinnitus also as an auditory object which is formed and processed by ASA in the early stages (5, 6). Tinnitus retains characteristics of various objects such as complex sound quality and typically has a defined spatial location (329, 557). However, as a phantom sound, tinnitus has no stored schema, meaning or explanation for the tinnitus and it does not interact with external sounds in typical ways, as observed in psychoacoustic masking studies (40, 41). Generalization of the object based on other senses is difficult as there is also no concurrent information arriving from other modalities, such as vision and/or touch, which can be used to corroborate and identify a sound source (343). These discrepancies disrupt later stage auditory object processing,
driving saliency of the tinnitus signal and making it difficult to habituate to (5, 6, 7, 344).

The ALT model defines aversive memory representations, reduced working memory capacity and strength of auditory prediction errors generated (also related to attention factors) as individual residual factors which can influence final magnitude judgments of tinnitus loudness and distress.

6.5.8. Prediction error and tinnitus

According to the theoretical paper by De Ridder et al. (4), deafferentation at the peripheral auditory level results in missing input reaching the cortex for certain frequencies. If this deafferentation is sufficiently large, prediction error occurs. Subsequent central plasticity processes attempt to compensate for this prediction error, including neuronal hyperactivity, synchronized neural activity, cortical map changes and memory retrieval, ultimately giving rise to the sensation of tinnitus. Reduced sensory input and incomplete memory updating can correspond with decreased alpha-band activity, increased beta activity for prediction error propagation and increased gamma activity within functional tinnitus regions in the cortex (67). With limited deafferentation, missing information can be retrieved from neighbouring auditory cortical regions (67). However, if the deafferentation spans across many frequencies, missing information may be retrieved from parahippocampal auditory memory using theta carrier waves; persistent theta-gamma coupling may form the neural basis for conscious perception of tinnitus (67, 301).

The role of prediction error in tinnitus generation and maintenance has only just begun to be empirically studied. Roberts et al. (558) reviewed how auditory attention focused on this prediction error due to missing auditory input may result in the neuroplastic changes of tinnitus. Two studies examined MMN responses between tinnitus and matched normal-hearing controls and reported significant MMN amplitude reductions for pitch, duration and silent gap deviants among the tinnitus group (237) and for frequency deviants located at the audiometric normal lesion-edge (559). De Ridder et al. (7) reported 97% of tinnitus patients who remembered their dreams after rapid-eye movement (REM) sleep did not perceive tinnitus while dreaming. Factors such as the absence of P3 and incomplete structure of the MMN in sleep compared to wakefulness (526) suggest that predictive processing may be disrupted during sleep, therefore prediction errors may not be elicited in this state. However,
this remains as indirect, speculative evidence. It would be beneficial to measure behavioural responses or design objective methods of measuring neural prediction processes in the tinnitus population and compare this to control groups to detect differences.

Studies examining oscillatory activity in tinnitus have been conducted, and to date, show largely contradictory findings. Weisz et al. (549) found reduced resting state alpha-band and increased delta-band activity among tinnitus participants, especially in the right temporal and left frontal areas, when contrasted with normal hearing controls. These activity levels significantly correlated with the extent of tinnitus distress. Adamchic et al. (144) found higher delta, theta, beta, and gamma-band activity, and lower alpha-band activity among the tinnitus patients group compared to healthy controls. Mohan et al. (560) examined 311 tinnitus patients and 256 healthy controls and found distinct brain networks to be active and different network connectivity for all frequency bands (except gamma) between the two groups; the neural networks considerably overlapped in the gamma band frequencies. Increased levels of theta-gamma coupling among tinnitus patients has been observed using electroencephalography (EEG) (83, 145) and magnetoencephalography (MEG) (149, 150, 561) as well as intracranial recordings(251). Some studies report oscillatory activity differences as follows: in the beta-band range (562, 563), the gamma band (561, 564, 565) or alpha band (292, 561). Other studies did not find any changes in beta or gamma-band activity (292, 549, 566-570) or any changes in alpha-band activity (100, 230, 562, 564-571) among individuals with tinnitus.

Correlation analysis between oscillatory band activity and tinnitus characteristics have also been conducted. Strong positive correlations between subjective tinnitus loudness and resting-state contralateral auditory cortex gamma-band activity (145), temporal region delta-band activity (572), theta-band activity in secondary auditory regions (146, 154), anterior insula alpha-band activity, anterior cingulate cortex beta-band activity and parahippocampal gamma-band activity (83) have been demonstrated. For narrow-band noise (NBN) tinnitus, tinnitus laterality corresponded with gamma band levels in the contralateral parahippocampal region. NBN tinnitus also resulted in lower delta and increased beta and gamma-band activity within the lateral frontopolar cortex, the posterior cingulate cortex and parahippocampal areas when compared to pure-tone tinnitus (100). Vanneste et al. (154) observed increased bilateral gamma band activity in the auditory cortices irrespective of tinnitus laterality (right, left, both ears). Parahippocampal gamma activity and auditory cortex activity was linked by theta-
gamma cross-frequency coupling (83). Pierzycki et al. (573) however found whole scalp resting state EEG oscillatory activity did not correlate with behavioral (either psychoacoustic or psychosocial) measures of tinnitus.

6.5.9. Working memory and tinnitus

Compromisation of working memory space, which occurs in the presence of tinnitus, can hypothetically affect the accuracy of predictive processing. Andersson and McKenna (8) systematically reviewed the relationship between tinnitus and cognitive functioning and concluded that the presence of tinnitus had most impact on cognitive task performance with low or high demand; medium demand tasks were not affected to the same extent. The authors suggest that tinnitus distress arises due to cognitive deficits (working memory and attention limitations), emotional processing bias and negative appraisal.

Persons with tinnitus have displayed impaired performance compared to non-tinnitus persons on various formal working memory and/or attention tasks including: reduced auditory verbal working memory, reduced divided attention performance (2), deficits in learning, rates of learning, immediate recall of words, serial encoding (9) dual tasks of attention, verbal fluency, short-term and long-term memory, reaction time (6), decreased autobiographical memory (related to self and self-understanding) (5, 10) and diminished performance on Stroop tasks measuring selective attention (11). In a study examining memory performance under the presence of external noise, Andersson et al. (12) observed the tinnitus group scored significantly lower on a digit-symbol test with intermittent masking playing in comparison to continuous masking, while controls scored significantly lower with intermittent masking compared to both silence and continuous masking. However, another study testing serial recall observed no differences between tinnitus and matched control groups under identical background noise conditions, indicating potential task-specific effects (13).

Individuals with tinnitus might utilize different compensatory memory strategies compared to controls (14). The nature of the cognitive task itself also plays a part in the level of difficulty experienced (3). More well-designed studies may enable for identification of the precise processes which show interference because of tinnitus. Even in instances where there was no
immediate decline in performance, possibilities exist for tinnitus to influence long-term performance if the task was to more persistent (e.g. at work for a whole day).

6.6. Conclusions

Chronic tinnitus is a complex phenomenon which debilitates quality of life in 15-20% of those who experience it. Certain aspects of tinnitus and external sounds neural processing are analogous and external sound processing relies significantly on regularity detection and anticipation for economical functioning. This narrative account of literature was conducted in order to review literature on auditory prediction, and examine the feasibility of a relationship between auditory memory, predictive coding and tinnitus generation and distress.

The predictive coding model based on the Bayesian brain hypothesis and top-down feedback serves as the fundamental framework in current literature for how auditory prediction may occur (Figure 16). This may rely on the presence of inhibitory neural templates within the auditory system. Redundant acoustic signals are cancelled whereas novel signals are enhanced and encoded further. A hierarchical nature of regularity detection and prediction is present, with earlier processing involving low-level regularity detection and streaming, while later cortical processes generate predictions (corresponding with MLR and late responses (e.g. MMN) respectively). Evidence for auditory predictive processing exists in the domains of speech (especially in instances of degraded speech quality or missing speech segments), music perception and in the identification of sound identification patterns in auditory object analysis. Attention appears to modulate the strength of predictions; however, it is not a necessary component of predictive processing itself. Much of what is understood about deviance detection comes from electrophysiological studies using the mismatch negativity waveform under the oddball paradigm. However, limitations may apply when extrapolating findings from MMN studies as it does not appear to reflect prediction error exclusively; also, the paradigm is inappropriate for modelling more complex real-life auditory phenomenon. There is empirical support for various cortical oscillatory bands to be involved in the transfer of prediction errors to higher-order regions as well as in top-down feedback of generated predictions.
Tinnitus may also be an auditory object which is formed and processed by ASA in the early stages. Certain discrepant characteristics between tinnitus and external sound potentially disrupt later stage auditory object processing, driving saliency of the tinnitus signal and making it difficult to habituate to. De Ridder et al. (7) suggest that constant prediction error and attentional focus can arise from missing auditory input, subsequently triggering the
central compensatory processes thought to generate tinnitus. Few studies have directly examined the role of prediction error in tinnitus; the majority of studies have examined oscillatory band activity changes with tinnitus and this has shown largely contradictory findings. Behavioural differences and objective methods in detecting deviances for sounds corresponding to sensory deafferentation should also be investigated between tinnitus and non-tinnitus individuals. Cognitive deficits (working memory and attention related) have been consistently observed among tinnitus sufferers, which can hypothetically be detrimental to optimal predictive processing. It is possible that all these factors - aversive memory representations, reduced working memory capacity and strength of auditory prediction errors – may be residuals (5) which can vary in levels between individuals and therefore determine the final tinnitus magnitude judgement.
Chapter 7. The short-term effects of Predictable and Unpredictable surf-like sounds on tinnitus adaptation
7.1. Preface

Publication

This chapter includes content from the article “The short-term effects of predictable and unpredictable surf-like sounds on tinnitus adaptation” submitted for publication in Acta Acustica United with Acustica.

What was undertaken?

A short-term adaptation experiment was conducted in which loudness level matches and tinnitus loudness and distress ratings (on a scale of 1-10) were obtained after four experimental conditions: baseline measure in silence, 30 minute presentations of predictable (tinnitus audible and inaudible in a repetitive manner) amplitude-modulated surf sound, unpredictable (tinnitus audible and inaudible in a randomized manner) amplitude-modulated surf sound and silence. Short-term exposure to unpredictable sounds affected tinnitus perception more, as measured using tinnitus loudness and distress ratings, than Predictable sounds. Loudness level matches did not change. A two-week feasibility sound therapy trial was administered in which participants took home predictable and unpredictable sounds for two weeks. Participants reported the computer-generated sound sounded static and as not pleasant to listen to over long periods of time.

Why was this needed?

There is theoretical support for the hypothesis that tinnitus perception and distress may be driven by constant prediction errors, however empirical examination of this theory has not been conducted to date. Despite being common and having being used as a therapy for many years there is no consensus as to the most appropriate sound parameters for tinnitus therapy, or if the treatment provides benefit over counselling alone. Predictability as a parameter of sound therapy stimuli on tinnitus has also not yet been studied. It is possible that the random nature of dynamic sounds may lead to greater informational masking of tinnitus than constant sounds, and this warrants further investigation. Surf sounds are advantageous as they allow for amplitude to be modified to various degrees, have been used within various clinical settings (e.g. for pain relief) and can resemble nature sounds to an extent.
How does it contribute to the objectives of the PhD?

Prediction is a residual factor under the ALT model. The results of this study suggest that short-term administration of unpredictable sound presents the auditory system with greater novelty and prediction errors during processing compared to predictable sound. Greater attention shifts and informational masking may result, which creates a facilitating effect in reducing tinnitus AL weighting overall by increasing the weighting given to residual and external sound components and decreasing tinnitus component weighting. This effect is additional to the shift in AL away from tinnitus and towards external sound in general. The results provide support for the tinnitus as prediction error hypothesis. However, this experiment did not control for other contributory effects (e.g. greater relaxation to one sound over the other, different emotions evoked by the two sounds, anticipation). The feasibility trial also highlighted certain issues with current stimuli, such as sounding static and not blending into the environment. A randomized clinical trial was subsequently developed and administered, discussed in Chapter 9 taking into account these considerations. This was a longer-term trial of 8 weeks, involving the comparison of dynamic environmental sound therapy stimuli to steady-state white noise. Various tinnitus and tinnitus-related psychological intervention outcomes were measured at multiple time points.
7.2. Abstract

**Objectives:** The complex nature of tinnitus and its interaction with sound requires research to better understand the contribution different sound characteristics make on tinnitus perception. This study compared the effect of predictable or unpredictable amplitude-modulated sounds on tinnitus. With predictable or steady-state sound stimuli, the tinnitus is masked/unmasked at regular intervals. It was anticipated that this will result in less adaptation to tinnitus over time when compared to unpredictable sounds.

**Study Design:** The study consisted of 2 parts. 1) A short-term adaptation experiment with 23 participants (14 male, 9 female, mean age = 58.6 years, SD = 12.8). Loudness level matches and rating scales for loudness and distress were obtained at a silent baseline and at the end of three counterbalanced 30 minute exposures (silence, predictable and unpredictable). 2) A qualitative two-week sound therapy feasibility trial with 7 participants (5 male, 2 female, mean age = 58.63 years, SD = 11.92). Participants took home a digital music player with the test sounds for two weeks and were interviewed at the end of the trial.

**Results:** Self-reported tinnitus loudness for the unpredictable sound was significantly lower than baseline ratings after acute exposure. Tinnitus annoyance ratings for the unpredictable condition were significantly lower than baseline; changes following the predictable sound condition were also significant but the effect was smaller. The feasibility trial identified participant preferences for sounds varied. A subgroup of participants did not obtain any benefit from either sound. For those participants who obtained benefit from the sound trial, the majority preferred unpredictable compared to predictable sounds. There were issues with sound therapy device handling.

**Conclusions:** Sound therapy stimuli in which tinnitus is made audible at unpredictable intervals may lead to greater reduction in tinnitus outcomes, than when audible at predictable intervals. User-friendly devices with manual volume controls may be better for administering the therapy in the long-term.
7.3. Introduction

Tinnitus is the perception of sound in the absence of sound in the environment (1-4). The precise mechanisms giving rise to tinnitus perception and distress are still under study, although it is now understood to be the consequence of lesion-induced plasticity in the central auditory system and associated cortical networks (2, 59, 78, 79, 128). It may undergo similar feature extraction, schema formation and semantic objective formation as external sound within the auditory system (5, 6). The complexity of influences on tinnitus also extends to effects of an individual’s culture, beliefs, work and social environments (6). Tinnitus magnitude has been hypothesized to be the result of interplay between spontaneous and driven auditory activity, personality, emotion, attention and prediction (5, 6, 10).

Tinnitus may occur as a result of auditory prediction error (4, 7, 550). Prediction of upcoming auditory events reduces environmental uncertainty and ensures that sensory processing is economical. Regularity detection is also critical in providing sequential processing cues during Auditory Scene Analysis (ASA) (69), in order to categorize incoming, overlapping sounds into distinct auditory objects (e.g. a car horn, human speech) (61, 68-70). These operate independent of attention and are thought to rely on Gestalt principles of perception (574) as well as top-down Bayesian processes, which are modelled on the hypothesis that in situations of uncertainty, the brain relies on internal probabilistic models to optimise function (497). Internal memory representations are present at each level of the sensory processing hierarchy; incoming sensory input is compared against this existing schema to generate predictions about what input may arrive in the near future (497, 575, 576). Only the difference or mismatch between the prediction and arriving subsequent input, the prediction error, is passed onto the next level for processing. As such, unpredictable sounds are given higher priority by the brain while predictable stimuli are not consciously processed as they lack novelty. Moreover, top-down projections from higher-order regions allows for internal memory representations to also be updated for future events (this is thought to occur by alterations to the receptive field properties of low-level sensory units) (489). Deafferentation at the peripheral auditory level results in missing input reaching the cortex for certain frequencies (7). According to De Ridder et al. (7, 67), if this deafferentation is large, topographically-restricted prediction error occurs. This may divert attention and increase tinnitus salience which, alongside other central plasticity processes (including neuronal
hyperactivity (2, 577), synchronized neural activity (578, 579), cortical map changes (96, 113) and memory retrieval (4) may contribute to the sensation of tinnitus.

A common observation regarding tinnitus perception is that it is often affected by sound (28, 29, 190, 191). Sound therapy, currently one of the most widely used paradigms for tinnitus management, introduces external sounds to modify tinnitus perception and/or reactions to it (5, 21, 113, 171). Sounds used include broad-band noise (BBN), narrow-band noise (either pitch-matched or unmatched to tinnitus), environmental sounds or music (28-30). Despite being common and having being used as a therapy for many years there is no consensus as to the most appropriate sounds for tinnitus therapy, or if the treatment provides benefit over counselling alone (20, 31, 32). In a study by Wolfgang & Christian (580) using 124 tinnitus outpatients, those who received low-level white noise sound therapy in addition to cognitive behavioural therapy (CBT) did not show any additional benefit to the CBT alone group.

BBN mixed with tinnitus the tinnitus is recommended with the Tinnitus Retraining Therapy (TRT) paradigm (185). BBN noise has a relatively flat noise spectrum which is proposed to be more easily tolerated, neutral in nature and better for facilitating habituation than tones or NBN (23, 185). Kim et al. (213) found that TRT using BBN lead to the highest improvement in tinnitus outcomes, followed by mixed noise (combination of both BBN and NBN) and NBN TRT respectively. Similar findings have been observed in other studies (22, 581). In an earlier controlled clinical study, Henry et al. (22) compared masking set by the individual and BBN TRT and recorded that both masking and TRT showed improvements over time, but TRT patients continued to demonstrate greater improvement after six months. On the other hand, Tyler et al. (26) demonstrated no difference in outcomes with different levels of sound. There is some evidence that dynamic sounds that temporally vary may provide greater masking benefit compared to fixed intensity sounds (29, 582-584).

It is possible that the unpredictability provided by dynamic sounds may lead to greater informational masking of tinnitus (168). This term describes the elevation of auditory thresholds in the presence of masking stimuli which cannot be accounted for by energetic masking alone (at the level of the cochlea) (171, 174). It is thought to involve central auditory processes, possibly due to competition for cognitive resources (171, 174, 176). Informational or “central” masking is possible with tinnitus as the phenomenon is due to central processing itself. The precise mechanisms of such masking is not completely understood, although as mentioned above, competing for the brain’s cognitive resources may be a key factor.
The Neuromonics Tinnitus Treatment (NTT) utilizes customized music (dynamic wide frequency stimulus) and counseling, which promotes relief and relaxation by engaging the emotional regions of the brain (216, 217). In the first stage of treatment, individuals have their tinnitus almost completely masked, before moving onto a second stage of intermittent masking (tinnitus is audible part of the time). After six months of intervention, Neuromonics group patients reported greater alleviation of tinnitus symptoms and greater user acceptability than those subjected to counseling and BBN, or counseling only respectively (216). In patients with greater levels of hearing loss, adaptation of the standard NTT treatment to extend the first stage of stimulation by 2 months has shown greater reduction in clinical distress than applying the standard treatment (25).

Nature sounds also offer considerable dynamic variability with complex frequency components that vary in level. Schreitmüller et al. (220) observed that nature sounds, even though they presented with higher dynamics and higher masking thresholds, were more accepted by the listener than white noise. The relevance of the stimuli to the individual’s everyday environment may be a reason for it being easily tolerated. Ocean or wave sounds have recently been introduced by several hearing aid manufacturers in their tinnitus therapy devices (221, 222). Surf sounds vary in their temporal characteristics, and have been advocated as being useful for pain relief in various clinical populations (223-225), relaxation of breathing (226) and lowering blood pressure (227) and enhancing sleep quality among critical care unit patients (228).

The complex nature of tinnitus and its interaction with sound requires research to better understand the contribution different sound characteristics make on tinnitus perception. The aim of this behavioural study was to provide preliminary evidence of the relative effect of predictable and unpredictable amplitude-modulated “surf-like” sounds on tinnitus characteristics of loudness and distress/annoyance. With predictable or steady-state sound stimuli, the tinnitus is masked/unmasked at regular intervals. It was anticipated that this will result in less adaptation to tinnitus over time when compared to unpredictable sounds.

7.4. Methods

The methods were approved by the University of Auckland Human Participants Ethics Committee.
There were two parts to this study: a short-term adaptation experiment and a two-week feasibility sound trial using the test stimuli. The adaptation experiment aimed to measure quantitative changes in tinnitus loudness and distress, while the feasibility trial was included to provide broader subjective, qualitative views from listeners about the stimuli and feasibility of the methods for a plan longer term intervention trial.

7.4.1. Short-term adaptation experiment

7.4.1.1. Participants

For an effect size of 0.8, a minimum of 20 participants were needed in order to detect a one-point change in loudness on the rating scale (using normative data (M=6.066, SD =1.5) from a data set of 1094 tinnitus patients from the Tinnitus Archive, a research database set up specifically to study tinnitus characteristics, http://www.tinnitusarchive.org/dataSets/). Twenty-three participants (14 male, 9 female, mean age = 58.6 years, SD = 12.8) from the University of Auckland Tinnitus Research Volunteer Database were recruited. The inclusion criteria for the study were: aged over 18, have constant tinnitus, hearing in the normal to a moderate-severe loss range and normal middle ear function. A summary of participant characteristics is provided in Table 7.

7.4.1.2. Materials and Tests

**Stimulus:** Amplitude modulated “surf-like” sounds of 30 minutes duration were played through Telephonics TDH-50P supra-aural headphones. Predictable stimuli were simulated surf sounds, which altered +/- 2-5 dB in relation to the minimum masking level of the tinnitus, in order to make tinnitus audible at regular time intervals (Figure 17). Unpredictable stimuli were surf sounds which varied amplitude (maximally +/- 2-5 dB in relation to the minimum masking level of the tinnitus) and modulation rate in a manner such that tinnitus is audible at random time intervals. The long-term average loudness spectrums of predictable and unpredictable sounds were equivalent (Unpredictable Leq/total sound energy over 30-minute duration = 38.3 dB SPL; Predictable Leq/total sound energy over 30-minute duration = 38.7 dB SPL) (Figure 18).
Table 7. Participant characteristics for short-term adaptation experiment. Participants with ‘*’ took part in the two-week sound trial.

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</table>

The two modulated test stimuli for this study were compared along time and frequency domains to three ocean surf tinnitus relief sounds (Ocean 1, 2 and 3) currently used by a mainstream hearing aid company in their hearing aids. The Artificial Ear Type 43AC test-jig (calibrated before testing) was used, which complies with international requirements for acoustically testing sounds coupled to the ear. Test stimuli were set at the minimum masking level of a hypothetical individual with tinnitus at 3000 Hz (most prevalent psychoacoustic match of pitch in tinnitus groups (75, 81)), loaded onto an Apple iPod Shuffle Digital Music player (same model used for the feasibility trial) and the stimuli were played via Apple ear bud phones placed directly into the tapered opening of the test-jig. Ocean sounds were played into the test-jig using a mini RITE model hearing aid and tube inserts from the relevant hearing aid.
Figure 17. Theoretical diagram of modulated “surf-like” sounds in a predictable condition (above) with tinnitus audible in regular periods, and unpredictable condition (below) with tinnitus audible at random time intervals. Sound level fluctuations +/- 2-5 dB to minimum masking level of an individual’s tinnitus.

Figure 18. Comparison of Leq (total sound energy over the 30-minute duration) in dB SPL for predictable and unpredictable sounds demonstrating no significant differences between the two stimuli (Unpredictable (black) = 38.3 dB SPL, Predictable (white) = 38.7 dB SPL).
Power spectrum density analysis (dB SPL/Hz) showed that the ocean sound had smoother frequency spectrums, with relatively equal signal strength across frequencies (average = 15 dB SPL variation) (Figures 19 and 20). In contrast, both the modulated test stimuli for this study showed peaks typical of sinusoidal waves. The traditional surf-sounds were closer to white noise which gives a flat power spectral density. The test stimuli are more dynamic in this regard compared to those used in hearing aids currently. Sound level (dB SPL) variation for Ocean sounds 1 and 2 is greater compared to both predictable and unpredictable test stimuli. Ocean 3 did not show much variation over time. The test stimuli fell in between the various surf sounds in terms of the temporal dynamic nature. It is noted that absolute output sound levels may be different due to transducer voltage output differences between headphones and hearing aids.

**Study Design:** Pure tone audiometry and tympanometry were conducted to evaluate participants relative to inclusion criteria. Audiometry (0.25 – 16 kHz) was undertaken using a modified Hughson Westlake procedure (585) with a two-channel Grason Stadler GSI-61 audiometer. Measurements were undertaken using Telephonics TDH-50P supra-aural earphones (0.25 – 8 kHz) and high frequency circumaural Sennheiser HDA-200 headphones (9 – 16 kHz). Baseline psychoacoustic matching was carried out to determine natural individual characteristics of tinnitus, using tinnitus testing software (The University of Auckland ®) under high frequency circumaural headphones (Sennheiser HDA-200). Tinnitus pitch match was assessed throughout the test frequency range of 0.25 – 16 kHz using the two-alternative forced-choice (2AFC) method. Each tone was presented at a sensation level of 15 dB SL. Pitch match was then compared to tones one octave above and below to rule out octave confusion. The measurement was repeated until two repeatable responses were obtained. Loudness level matching was obtained using the pitch-matched stimulus sound at 30 dB above the threshold level and decreasing it slowly in 2 dB steps until the participant stated it was same loudness as their tinnitus. This was repeated three times, and the average of the last two runs was taken.
Figure 19. Unweighted power spectrum density plots (dB SPL/Hz) for three ocean surf sounds currently used in hearing aids as tinnitus therapy ((A) Ocean 1, (B) Ocean 2 and (C) Ocean 3) and for predictable and unpredictable stimuli used in this study ((D) Unpredictable and (E) Predictable).
Figure 20. Time spectrum for three ocean surf waveforms currently used in hearing aids as tinnitus therapy ((A) Ocean 1, (B) Ocean 2 and (C) Ocean 3) and for predictable and unpredictable waveforms used in this study ((D) Unpredictable and (E) Predictable).
This was subtracted from the threshold level, to obtain a level match in dB SL. Minimum masking level (MML, in dB SL) was obtained using a NBN stimulus, raising it from threshold level until the participant reported that the tinnitus was no longer audible. This procedure was repeated three times, and the average level was calculated. This was subtracted from the threshold level to give the MML match in dB SL.

Participants were exposed to four experimental conditions always beginning with a baseline measure (tinnitus measurements taken in silence immediately upon the participant arriving), followed by 3 presentations of predictable, unpredictable and silence with the measures repeated while seated in a comfortable chair in a well-lit, sound-proof booth. Conditions were counterbalanced: condition 1) 30 minutes of silence with no sound stimuli playing but with the supra aural headphones on, condition 2) 30 minutes of predictable sound, and condition 3) 30 minutes of unpredictable sound. Participants were informed at the beginning of the study that their tinnitus measurements will be taken at equal intervals of time, either immediately following a period of quiet for 30 minutes or listening to computer generated surf sound for 30 minutes. At the end of each experimental condition, participants were asked to provide ratings of their current tinnitus loudness and distress on a 10-point scale (Loudness: 1 = tinnitus is not audible, 10 = tinnitus is very loud; Distress: 1 = tinnitus is not at all annoying and/or distressing, 10 = tinnitus is very annoying and/or distressing) as well as match tinnitus loudness level using the tinnitus testing software. For Conditions 2 and 3, tinnitus ratings were taken at the end of 30 minutes while the stimulus was still playing (sound-on) and again immediately after the stimulus was switched off (sound-off). This resulted in six tinnitus loudness and distress measurements (baseline, quiet, predictable sound-on, predictable sound-off, unpredictable sound-on, unpredictable sound-off) and four tinnitus loudness level matches (baseline, quiet, predictable, unpredictable) in total for each participant. While baseline and silent condition measurements were similarly taken in the absence of sound in the same conditions, they were both included in the analysis as it is acknowledged that silent condition measurements may be (at least partially) affected by preceding sound therapy stimuli (10).

7.4.1.3. Statistical analysis

Repeated measures ANOVA were used to examine tinnitus loudness and distress ratings between the four experimental conditions (baseline, quiet, predictable sound-off,
unpredictable sound-off); loudness level matches between conditions were also compared using the same test. Pearson correlations and paired samples t-tests were used to examine correlations between sound-on and sound-off tinnitus loudness and distress ratings.

### 7.4.2. Feasibility trial

Ten participants from the first study were randomly selected for the feasibility trial using an online, free True Random Number Generator (https://www.random.org/). Each participant was given a code number from 1-23 Participants whose codes matched the first 10 generations of the random sequence were invited to take part in the two-week sound trial. Seven participants (5 male, 2 female, mean age = 58.63 years, SD = 11.92) accepted and took part in the final trial. Participants were provided with Apple ear bud phones and an Apple iPod Shuffle Digital Music player with the sound stimulus from the experiment loaded. Participants were instructed to listen to one track for the first week (predictable or unpredictable in counter-balanced order), take 5 days rest and listen to the next track for the following week. They were encouraged to listen to the sounds whenever needed (i.e. whenever tinnitus is loud and/or bothersome). No minimum or maximum time limits were imposed for listening. Participants were asked to keep written notes of their sound track usage throughout the trial. At the end of the sound trial, participants provided their written notes and were interviewed. The interviews were digitally recorded, transcribed, and responses coded into themes. The interview schedule is provided in Table 8.

The framework method (586) was used to analyse the interviews, consisting of five steps: familiarization, identification of a thematic framework, indexing, charting, and mapping and interpretation. Familiarization involved careful listening to the digital recordings and transcribing, and re-reading the transcription. Common themes were identified in the transcripts, and in the charting phase, the data was rearranged according to theme. In the mapping and interpretative stages, the charted data was compared and contrasted to identify patterns within the data. Both authors independently coded responses into themes, these were then compared against each other and the final themes were agreed for rearranging data.
Table 8. Interview schedule for feasibility trial.

| 1. How often did you use sounds stimuli? |
| 2. In which particular environments did you find yourself using the sounds? |
| 3. Which sound did you use more during the two weeks? Why? |
| 4. Which of the two stimuli (predictable or unpredictable) did you prefer the most? Why? |
| 5. How are the two sounds different to each other? What were the advantages and disadvantages of each of the two sound stimuli? |
| 6. Will you be willing to wear this device as a form of tinnitus management for the next 6 months? Why or why not? |
| 7. How can each of the sound stimuli be improved and why would this be an improvement? |
| 8. Any other comments? |

7.5. Results

7.5.1. Short-term adaptation experiment

There were significant differences in tinnitus loudness ratings at the end of the four conditions (baseline, predictable, unpredictable, silent) taken with the sound stimulus switched off (F(3,66)=4.843, p < 0.05). Tinnitus loudness ratings following administration of unpredictable sounds were significantly lower than baseline (Figure 21). There was a significant difference for tinnitus annoyance ratings at the end of the four conditions taken with the sound stimulus switched off (F(1.805,39.7)=5.802, p < 0.05) after a Greenhouse Geisser correction was applied following violation to the assumption of sphericity (X²(3) =20.561,p < 0.05; ε = 0.602). Tinnitus annoyance rating following administration of unpredictable sounds was significantly lower than baseline; tinnitus annoyance rating following predictable sound administration was significantly lower than baseline as well but to a lesser extent (Figure 22). There was no significant difference for loudness level matches.
between conditions after a Greenhouse Geisser correction was applied following violation to the assumption of sphericity ($X^2(3) = 17.457$, $p > 0.05$; $\varepsilon = 0.648$).

**Figure 21.** Tinnitus loudness ratings on a 10-point scale across the four experimental conditions. A significant difference was found between loudness ratings taken after the unpredictable condition compared to baseline (indicated with *). Error bars represent +/- one standard error.

**Figure 22.** Tinnitus annoyance ratings on a 10-point scale across the four experimental conditions. A significant difference was found between annoyance ratings taken after the unpredictable condition when compared to baseline; and between the predictable condition when compared to baseline (indicated with *). Error bars represent +/- one standard error.

There were significant positive correlations between sound-on and sound-off measurements for tinnitus loudness ratings for the predictable condition ($r = 0.889$, $p < 0.05$), tinnitus
loudness ratings for the unpredictable condition ($r = 0.637$, $p < 0.05$), tinnitus annoyance ratings for the predictable condition ($r = 0.685$, $p < 0.05$) and tinnitus annoyance ratings for the unpredictable condition ($r = 0.902$, $p < 0.05$). There was a significant difference between tinnitus annoyance with the sound on compared to sound off ratings, with sound on annoyance ratings for the predictable condition ($M=4.3$, $SD=0.463$) being slightly louder than sound off annoyance ($M=3.4$, $SD=0.456$) (Figure 23).

**Figure 23.** Tinnitus loudness and annoyance ratings taken at the end of 30 minutes exposure with the sound stimulus playing (sound-on) and sound stimulus turned off (sound-off) for Predictable (P) and Unpredictable (UP) conditions. Significant differences indicated with (*). Error bars represent +/- one standard error.

### 7.5.2. Feasibility trial

Following qualitative analysis using the framework method, certain key areas emerged with regards to the sound trial. There was a divergence of individuals into those who obtained benefit from the sound therapy and those who didn’t. For those who had benefited from sound therapy, there was a preference of unpredictable over predictable sounds. The situations in which sound therapy was used were common. There were limitations due to the
sound therapy device; sound administered through earphones via iPod. Participants did not believe it to be practical in a long-term intervention.

7.5.2.1. Environments of use

The majority of participants used the sounds during the evening time or before bed.

“At home in the evening. Either in the lounge or in bed.”

“Almost exclusively in a quiet environment, while reading a book in bed before going to sleep.”

A few participants preferred to use it while they were using their computer, walking, at the gym and driving. One participant described the tinnitus as not being evident when the sound tracks were played when simultaneously doing other activities, but begins to become evident if the sound tracks were playing in quiet.

7.5.2.2. Sound Therapy Preference and Benefit

All the participants reported using both sound tracks equally, the main reason being that was what was instructed of them. Of the 7 participants, 3 participants preferred the unpredictable sound, 1 preferred the predictable sound and 3 did not prefer either or preferred quiet instead of the sound tracks.

Unpredictable preference

“The unpredictive blocks the tinnitus better I feel and is a more natural sound. This was easier to listen to as it resembles the sound of the sea shore. The predictive sound was hard to listen to at first but I soon was ignoring it.”

“Although I did not find the difference very dramatic, the unpredictive sounds seemed less “obvious” to me, while I was reading. It seemed to me that with the predictive sounds, I paid more attention to them in the background, because I “knew” that they were varying according to a fixed pattern.”
Predictable preference

“They are significantly different for blocking tinnitus. It was more effective, for 1st one (unpredictable), the tinnitus was trying to fight over it.”

For those who did not prefer either sounds, the sound stimuli tended to be intrusive or direct attention towards to the tinnitus, exacerbating it.

“The quality of both sounds are static anyway and neutral. I think I was more conscious of it then I was thinking about it. Not drawing attention towards the tinnitus. With the sounds, tinnitus is audible. Tinnitus gets louder with background sound, e.g. louder with radio. When absorbed in tasks, tinnitus isn’t evident.”

“The sounds are novel, so end up paying attention to it as intrusive, unfamiliar noise.”

7.5.2.3. Long-term use of sound device for tinnitus management

Two participants said they would prefer and 4 participants that they would not prefer to wear this device as a form of tinnitus management for the next 6 months (1 participant did not respond to this question). A common reason reported by participants for not wanting to adhere to long-term management was the set up of the shuffle device, with a single button control, which made it difficult to switch between the two tracks or set volume.

“I found it difficult to get a loud enough volume and as I set all up time consuming and uncomfortable. As not loud enough, tended to have speaker or ear plugs too close to body i.e. rolled on, etc.”

“Was difficult to change the volume.”

“I see merit in what you propose, but feel a more sophisticated ‘delivery system’ required.”
7.6. Discussion

This study compared sound stimuli in which tinnitus became audible and inaudible in a predictable repetitive manner and unpredictable randomized manner to see which was more effective for tinnitus sound therapy. After short-term administration of 30 minutes, tinnitus loudness ratings were significantly lower for unpredictable sounds in comparison to baseline loudness ratings. There were no significant differences between baseline and the silent condition or predictable condition. Tinnitus annoyance ratings were also significantly lower for unpredictable sounds than baseline; predictable sounds were also significantly lower than baseline but the effect was smaller. Although there was a divergence of opinion, more participants preferred the unpredictable sound over the predictable during the two-week sound trial. These results suggest that a controlled clinical trial would be an appropriate next development in this research.

The results are discussed in terms of how these sounds may have resulted in changes in prediction and prediction error processes in the auditory system, informational masking (174) as well as tinnitus adaptation level (AL) changes (5). However, the authors do acknowledge that there may be other contributory effects (e.g. greater relaxation to one sound over the other, different emotions evoked by the two sounds, anticipation) which can exert additional influence. Controlling for/measuring these various side factors in a clinical trial setting is therefore critical to further strengthen our findings. Surf sounds with amplitude modulating in a regular pattern may enable the auditory system to extract and set up temporal regularities (60, 61), and as long as these regularities are maintained, familiar signals are not attended to and the brain undergoes habituation to it in the long term (493). In contrast, unpredictable sounds, due to their random modulated amplitude and rate, would continue to elicit prediction errors and attention processes may be diverted to processing of this sound instead of the tinnitus. Greater informational masking of tinnitus may be provided by unpredictable sounds compared to predictable sounds due to the random nature of the prior sound (38, 171). This can lead to an increased cognitive load presented to the system (unpredictable sounds supply their own novel deviants) and can disrupt the ability to focus attention selectively on any particular auditory stream (7, 38, 171). As such, detection of tinnitus prediction errors may be reduced.
Electrophysiological evidence indirectly supporting this include an enhancement of the P3 component, related to attention orienting processes, when a deviant stimuli is introduced (258, 283) and the commonly observed Mismatch Negativity (MMN) component which is typically elicited 100–200 ms in the frontocentral regions after onset of auditory input which violates the regularities set up by preceding sequences (260, 274, 282). Informational or “central” masking is possible with tinnitus as the phenomenon is due to central processing itself (2, 34). The precise mechanisms of such masking are not completely understood, although as mentioned above, competing for the brain’s cognitive resources may be a key factor (38, 168). Such masking is efficient in a clinical setting as 1) the masker sound does not have to be frequency specific, 2) unilateral tinnitus can be masked by contralateral sound and 3) tones can mask tinnitus described as being broadband in nature (42).

Another interpretation is in terms of adaptation level (AL) (5, 6). The AL is defined as the body’s internal anchor or reference point according to the adaptation level theory (ALT) framework for tinnitus. In the short-term experiment, increased attention and auditory processing allocated to the unpredictable stimuli has the potential to shift the AL away from the tinnitus and towards the background noise. As a result the AL for tinnitus is lowered and it is reduced in audibility and affect. Short-term adaptation to sounds consistent with the ALT hypothesis have been demonstrated previously (10). If presented for a long-term, these perceptual changes are hypothesized to be sustained.

The only potential issue which may arise with intermittent masking such as that used in this study is the auditory continuity illusion (485) whereby over time, we learn to ‘fill in the gap’ where masking sound is applied, such that tinnitus is heard as a continuous percept throughout. This learning effect involves several networks in the brain which overlap with that of tinnitus, including the limbic structures, basal ganglia and prefrontal cortex (587).

Davis et al. (588) observed more consistent benefit over 12 months if NTT involved masking of tinnitus for the first two months followed by intermittent perception of tinnitus compared to where there is intermittent perception of tinnitus throughout treatment. It is anticipated that this continuity effect will not occur for stimuli which vary significantly over time, but there hasn’t been any research conducted in this area that we are aware of. Moreover, the effect of degree of hearing loss also needs to be taken into consideration – extended constant masking showed greater reduction in tinnitus distress for those with higher levels of hearing loss in the study by Távora-Vieira et al. (25). While subjective ratings of tinnitus changed, the objective loudness level match measures did not differ across conditions. Similar effects have also been
observed in long-term tinnitus treatments, with significant subjective but negligible objective loudness changes of tinnitus (39). Searchfield et al. (6) stress that loudness ratings and LLMs are two different constructs and may utilise different reference points. Tinnitus LLMs are matched against an external sound as a reference point, while subjective loudness ratings are made in silence. Furthermore, self-perceived tinnitus magnitude is affected by various higher-order psychosocial factors and is proposed to be a combination of loudness, severity and tinnitus awareness (4, 6, 83, 158).

The results of the two-week sound trial have brought to attention considerations for administering these stimuli as a potential tinnitus intervention. For a subgroup of individuals, the presence of a new sound was not beneficial and made the tinnitus more prominent. In these individuals, the external sound itself may be annoying and/or trigger negative reactions. Negative emotions can exacerbate tinnitus by co-activation of cortical networks (3, 8, 59, 78). A limitation and possible confound however might be that the device itself was difficult to use (single control button for setting volume and changing tracks), leading the majority of participants who took part in the trial to not want to use this in the long term. Future considerations will be to administer a long-term clinical trial of at least three months using more practical devices such as behind-the-ear hearing aid devices, or digital music players with display screens, with different volume control and program toggles. In order to study the influence of emotional affect on the effectiveness of dynamic sounds, nature surf sounds and more static environmental sounds will be compared to predictable static sounds (e.g. BBN). It is anticipated that the presence of pleasant, relaxing environmental sounds will have an additional benefit for tinnitus reduction. This emotional benefit can be measured using questionnaires, interviews, etc.

7.7. Conclusions

Both the short-term adaptation study and sound trial results from this study indicate that sound therapy stimuli, in which the tinnitus is unpredictable in nature, may be more beneficial than predictable tinnitus stimuli for the reduction of tinnitus loudness and distress/annoyance. Modelled under the ALT framework for tinnitus, this result is due to greater shift in attention and subsequent weighting towards the external sound, resulting in AL shifts away from the tinnitus. Participant preference for unpredictable stimuli may be due to greater informational masking, higher tolerance and resemblance to sounds in the everyday
environment, reflecting other studies into nature sounds. Future studies will look at objective measures of assessing differences in predictable and unpredictable tinnitus sound therapy stimuli, identifying ways for grouping individuals into those who would benefit from sound therapy and who would not, and in designing interventions incorporating these stimuli for long-term tinnitus relief. Such an intervention will potentially last at least three months and involve administration of dynamic sounds (e.g. nature surf sounds) and predictable static sounds via behind-the-ear hearing aid devices or digital music players in order to see which reduces the perception of tinnitus the greatest.
Chapter 8. Auditory streaming and prediction in tinnitus sufferers
8.1. Preface

Publication

This chapter includes content from the article “Auditory streaming and prediction in tinnitus sufferers” submitted for publication in Hearing Research.

What was undertaken?

Mean ERP amplitudes and oscillatory band activity of individuals with tinnitus and hearing-level matched controls were measured using EEG in response to tone deviants and tone omissions (at the pitch of tinnitus). A larger N1c waveform was elicited in the absence of any tone deviation within the left primary auditory cortex of tinnitus participants. Abnormal N1c waveform growth was present across levels of deviant conditions for tinnitus. No differences were present between groups for tone omissions. Different levels of activity between tinnitus and control groups were observed in regions corresponding to attentional as well as limbic networks. The only difference in oscillatory band activity was in response to tones 7 semitones different from tinnitus pitch, with significantly lower beta-2 band activity present for tinnitus, correlating most with activity within the right inferior occipital gyrus.

Why was this needed?

Two processes carried out regularly by the auditory system that largely depend on picking up regularities of incoming sound are auditory stream analysis (ASA) (to identify incoming sound sources) and anticipation of future events. Under this context, prediction errors can be elicited either due to deviance present in auditory input as well as omission of input. Despite theoretical support, there is an absence of studies directly examining the hypothesis of constant prediction errors driving tinnitus perception. This theory can be tested using electrophysiology as if tinnitus is driven by greater prediction errors following missing input, abnormal deviance waveforms would be observed for tone deviants and tone omissions in instances where the tone corresponds with frequencies at or near the site of deafferentation. Predictive processing may also map onto neural oscillatory activity (e.g. gamma activity transferring prediction errors to higher-order regions), however this is a debated area and further research is also warranted in this regard.
How does it contribute to the objectives of the PhD?

Prediction is a residual factor under the ALT model. The results of this study suggest that cortical-level auditory stream segregation may be disrupted among individuals with tinnitus at or near the frequencies corresponding to tinnitus pitch. Constant prediction error generation, along with top-down feedback, tinnitus salient characteristics and conflict with expectations of sound can lead to tinnitus recruiting attention and cognitive resources during the later stages of object processing, and compromise streaming segregation processing of external tones. Modelled under the ALT, weighting is increased towards tinnitus and residual components, resulting in overall AL weighting increase. This effect is greater than any shifts in AL away from tinnitus and towards external sound played. This disruption is prone to occur within ambiguous streaming regions, in which attention or contextual alterations can bias perception towards either coherence or streaming.
8.2. Abstract

**Objectives:** The aim of this study was to determine whether auditory segregation, streaming and predictive processing is affected in tinnitus sufferers compared to non-tinnitus controls with matched levels of hearing. It was hypothesized that tinnitus would result in abnormal Electroencephalography (EEG) responses to tone deviants and tone omissions than in controls for frequencies near the pitch of tinnitus and this should correspond with increased levels of cortical gamma and theta oscillatory rhythms.

**Design:** Sixteen individuals with tinnitus (10 men and 6 women, mean age=53.44, SD=12.92 years) and 14 control participants (8 men and 6 women, mean age=50.25, SD=18.54 years) took part in the study. A modified version of the ABA streaming paradigm (589), with repeating triplet pattern of two frequencies (A and B) presented as A-B-A, was used to examine deviant-related prediction error. Omission-related prediction errors were examined using a modified version of a tone-omission paradigm (64). Regions of interest were frontocentral, left frontal, right frontal and temporal lobes.

**Results:** A larger N1c waveform was elicited in the absence of any tone deviation within the left primary auditory cortex of tinnitus participants. No differences were present between groups for omissions. The only difference in oscillatory band activity between the two groups in this study was in response to tones 7 semitones different from tinnitus pitch, with significantly lower beta-2 band activity present for tinnitus, correlating most with activity within the right inferior occipital gyrus.

**Conclusions:** The findings from this study imply that cortical-level auditory stream segregation is altered among individuals with tinnitus.
8.3. Introduction

Tinnitus is the perception of sound in the absence of sound in the environment (1-4). The precise mechanisms giving rise to tinnitus perception and distress are still under study, although it is now understood to be mostly a consequence of deafferentation of peripheral auditory signals resulting in compensation or inadequate noise reduction in central processing pathways (2, 7-9). Hearing loss and hearing-related problems are common risk factors for more debilitating tinnitus (14). Tinnitus prevalence increases significantly with hearing loss (3, 15), especially sensorineural hearing loss and individuals with tinnitus also frequently complain about difficulties associated with hearing (16, 17). Moreover, tinnitus pitch often correlates with the region of greatest hearing loss (or peripheral deafferentation) in an individual (18, 19). Sensorineural hearing loss causes reduced audibility of low level sounds (no audibility of certain frequencies if the loss is severe enough (192)), diminished frequency discrimination and unnatural loudness growth (590) in addition to tinnitus perception. At a broader social and environmental level, these changes can translate to difficulty in communicating, social withdrawal and/or affective symptoms, such as anxiety or depression (188, 386, 434, 474). Therefore, it becomes difficult to separate out the consequences that are the result of hearing loss from those which are a result of tinnitus (6).

Two processes carried out regularly by the auditory system that largely depend on picking up physical determinants of incoming sound are auditory stream analysis (ASA) and related predictive processing of future events. In this study, we attempt to fill some of the gaps in current literature pertaining to auditory streaming and prediction in individuals with tinnitus using event-related potentials. ASA sequentially analyses and separates incoming sounds into distinct streams or auditory objects (e.g. water running, speech, a car horn, etc.) (61, 68, 70, 591). At a perceptual level, tinnitus has been modeled as an auditory object which may undergo similar feature extraction and streaming as external sound within the auditory system (5, 6). Psychoacoustic matching of the tinnitus signal is possible clinically as the tinnitus often has discrete frequency, intensity, bandwidth and timing characteristics (592), and in cases is so robust that it is resistant to masking by external sounds (593). However incongruences between tinnitus and the surrounding environment, lack of attributable source, salient characteristics, persistent magnitude and conflict with expectations of sound (40, 41), may mean that tinnitus has attention diverted towards it during the later stages of object analysis, and ASA processing is subsequently disrupted (5, 6, 78, 343).
The prevalent ABA stimulus paradigm developed by Miller & Heise (589) for examining streaming segregation consists of a repeating triplet pattern of two frequencies (A and B) presented as A-B-A. The ability to separate pitch patterns and the ability to distinguish between sentences spoken simultaneously by different talkers (e.g. the ‘cocktail party’ effect) may be mediated by similar underlying cognitive processes as those recruited by this paradigm (594). When the frequency difference between A and B tones is small, a single stream is perceived and a galloping rhythm is heard by individuals (auditory coherence) (Figure 24). As the frequency difference is increased, the two tones eventually become segregated and can be perceived as two different concurrent streams of A-A-A and B-B-B (auditory streaming). The frequency threshold at which this divergence occurs is termed the segregation threshold. For an intermediate A and B tone frequency differences, the percept is bistable and can spontaneously flip between coherence and streaming (595, 596); this may be driven by top-down decision making processes (597). Time build-up effects are also observed, with an increased probability of streaming occurring as sequences are played over time (598). Attention-independent enhancement of the N1c and P2 waveforms (electrophysiological indicators of deviance or event anticipation) (280, 599) have been observed in relation to the processing of ABA tones and are attributed to frontal and auditory cortex sources (Heschl’s gyrus) (61, 600, 601).

Prediction, the ability to forecast future auditory events based on regularity detection, may also be disrupted among tinnitus sufferers. The Bayesian brain predictive coding model (155) states that in situations of uncertainty, the brain relies on internal probabilistic models to optimize function. At each level of the sensory processing hierarchy, incoming sensory input is combined with existing internal memory representations to generate predictions (155, 497, 575, 576). The difference between the two templates (e.g. deviances and/or omissions), which defines the prediction error, is passed onto the next level for processing and allocated greater cognitive resources. Based on this latest sensory input, the internal memory representation is continuously updated and changes are passed via top-down projections to alter the receptive field properties of low-level sensory units for future events (489). Rapid predictive error processing has been observed within early stages of the auditory pathways (50-100ms after onset) using electrophysiology upon omission of expected tones (64). De Ridder et al. (7) suggest that if deafferentation is sufficiently large, topographically-restricted prediction errors may be continually generated. Attention resources are diverted, triggering compensatory central plasticity processes, including neuronal hyperactivity (2, 577).
synchronized neural activity (578, 579), cortical map changes (96, 113) and memories of sound (4) ultimately giving rise to the sensation of tinnitus. This activity might also feed-forward into tinnitus distress networks and exacerbate reactions to the signal.

Arnal & Giraud (552) implicate neural oscillations in sensory prediction processing, whereby gamma activity may transfer prediction errors to higher-order regions while top-down feedback information is nested on beta bands. Changes in characteristic frequencies of brain wave oscillations may ensue, with sensory deafferentation triggering an adaptive cascade of events to retrieve missing auditory input, e.g. such as that described by Thalamocortical

Figure 24. Three perceptions are possible in auditory stream segregation: coherence (both streams merge into one galloping rhythm), segregation (separation into tones A and B; this is a function of time separation and frequency separation of A and B) and ambiguity (region where perceptual bistability can occur, with final perception determined by contextual and attentional manipulations). The Temporal Coherence Boundary and Fission (Streaming) Boundary separate the perception of streaming and ambiguity, and ambiguity and coherence, respectively. Adapted from (602), p. 30.
Dysrhythmia (TCD) Theory (149). Specifically, spontaneous resting state alpha rhythms would decrease, and delta, gamma and theta band rhythms would increase, particularly in temporal regions relating to the edge frequency (7, 67, 150, 549). Persistent theta-gamma coupling also would occur, for recruiting and synchronizing long-distance neural networks (67, 301). However, to date there are contradictory findings from empirical studies regarding oscillatory band changes among individuals with tinnitus (573, 603).

In this study, we tested the hypothesis that streaming and early predictive processing is altered in tinnitus sufferers compared to non-tinnitus controls with group matched level of hearing loss. EEG was used to compare average ERPs and oscillatory band activity. Two predominant types of auditory prediction error were examined, that which was elicited by 1) deviance from an expected auditory stimulus (measured using a modified ABA paradigm) and 2) omission of expected auditory stimuli (in which predictive processing is disrupted, measured using a modified tone-omission paradigm (64)). The tinnitus group would be expected to have abnormal growth in N1c/P2 waveforms as frequency differences between A and B increased compared to controls; abnormal N1c/P2 waveforms would also be present in response to tone omissions. In both paradigms, increased prediction errors among tinnitus sufferers were hypothesized to correspond with increased levels of cortical gamma and theta oscillatory rhythms than controls. The frequencies of interest were at/near the site of greatest deafferentation for each individual, which corresponded with the pitch of the tinnitus and where the greatest difference between the two groups was most likely to be observed. The regions of interest were frontocentral and temporal sites, consistently associated with auditory streaming and preliminary prediction coding (61, 64, 65, 557, 600).

8.4. Methods

The methods used were approved by the University of Auckland Human Participants Ethics Committee. The electrophysiological streaming and prediction methods were based on Snyder et al. (600) and Bendixen et al. (64).

8.4.1. Recruitment

To be included in this study, individuals had to be over 18 years of age, and have: no more than a moderate hearing loss in both ears for audiometric frequencies less than 8 kHz, no
middle ear problems, no known psychiatric or neurological illness, no psychiatric history or history of: drug/alcohol abuse, head injury, seizures, headache. Those in the tinnitus group had to have constant tinnitus. Tinnitus group participants were recruited via email invitations sent out to the University of Auckland Tinnitus Research Volunteer Database (individuals with debilitating tinnitus who had volunteered for tinnitus studies and clinical trials related to tinnitus relief). Participants for the control group were recruited through the University of Auckland Hearing and Tinnitus Clinic database (case history identified them to have hearing loss in one or both ears but no tinnitus) and using posters in public spaces at the University of Auckland. For 1 tinnitus participant and 2 control participants, EEG recordings were contaminated by excessive artifacts (eye and muscle movement) and were excluded from analysis.

8.4.2. Participants

Data from sixteen individuals with tinnitus (10 men and 6 women, age range = 32-76 years, mean age = 53.44, SD=12.92 years) and 14 control participants (8 men and 6 women, age range = 22-78 years, mean age = 50.25, SD=18.54 years) were used in the final streaming experiment and data-analysis. The average tinnitus pitch match for the tinnitus group was 2000 Hz. There were no significant differences in hearing thresholds between the two groups across speech frequency ranges (250-8000Hz) (Figure 25).

8.4.3. Materials and Tests

The experiment was run in a dimly lit sound attenuating room. Participants were seated comfortably in an armchair and recordings were made in an awake state in a passive, non-attending condition (watching a muted subtitled film via the computer monitor). All hearing testing was carried out in a sound-treated booth (ISO 8253-1). Audiometry (0.25 – 16 kHz) was undertaken using a modified Hughson Westlake procedure (585) with a two-channel Grason Stadler GSI-61 audiometer. Measurements were undertaken using Telephonics TDH-50P supra-aural earphones (0.25 – 8 kHz) and high frequency circumaural Sennheiser HDA-200 headphones (9 – 16 kHz). Tinnitus testing was carried out using tinnitus testing software (The University of Auckland) under high frequency circumaural headphones (Sennheiser HDA-200). Tinnitus pitch match was assessed throughout the test frequency range of 0.25 –
Figure 25. Average right ear (A) and left (B) audiometric thresholds in dB HL of tinnitus (black marker) and control (grey marker) groups for frequencies 125-16000 Hz. Error bars represent +/- one standard error.

16 kHz using a two-alternative forced-choice (2AFC) method. Each tone was presented at a sensation level of 15 dB SL. Pitch match was then compared to tones one octave above and below to rule out octave confusion. The measurement was repeated until two repeatable responses were obtained. The mean pitch of the tinnitus group was calculated and computed as the test equivalent ‘pitch of tinnitus’ for the control group.
Electrophysiology measures were undertaken using 66 active surface electrodes (Biosemi ActiveTwo system, www.biosemi.com) placed on the scalp according to the international 10/20 system array through attachment to an appropriately sized Biosemi 64 electrode head cap with SignaGel electrode gel. An additional electrode was placed on each mastoid. All sound stimuli were presented via E.A.R Tone 3A Insert earphones (Etymotic research) and controlled using Presentation 17 ® Software (www.neurobs.com) run from a desktop computer. EEG signals were recorded continuously at a sampling rate of 8192 Hz and downsampled to 512 Hz. Off-line analysis was conducted using Brain Electrical Source Analysis (BESA) Research 6.0 ® Software (www.besa.de). Electrodes were re-referenced to an average reference montage. Each EEG recording was corrected for eye blink and movement artifacts using the adaptive model approach in BESA. All ERP waves were digitally filtered with a 1 Hz, 12 dB/octave forward high-pass filter. For ERP amplitude analysis only (not sLORETA analysis), a 30 Hz, 24 dB/octave zero phase low pass filter was applied following epoching and averaging. A 60 Hz notch filter was applied to reduce line noise. The LORETA-KEY (v.20151222) software package as provided at www.uzh.ch/keyinst/LORETA.html, was used to carry out source localization and oscillatory band analysis. For ERP amplitude analysis an average referenced electrode montage was used, in which ERP mean amplitudes for activity at each electrode site was calculated separately.

**Desired Listening Level (DLL) Task**

For each participant, a Desired Listening Level (DLL) task was administered to determine a comfortable and readily audible sound level for each sound stimulus 1) at tinnitus pitch (Hz) and 4, 7 and 10 semitones lower than tinnitus pitch for the streaming experiment, and 2) at tinnitus pitch and 1500 Hz, 2000 Hz, 3000 Hz and 4000 Hz higher and 750 Hz, 500 Hz, 250 Hz and 125 Hz lower than tinnitus pitch for the prediction experiment. For each sound, the task began by presentation at the highest attenuation level possible (0.95, output level = 0 dB HL, inaudible) and decreased it in 20 steps to the least amount of attenuation (0.00). The sound stimulus would increase in loudness by 5 dB for each step until the participant pressed the space bar on the computer keyboard to indicate the DLL. This action would result in the intensity dropping by 10 dB and increasing again until the participant indicated DLL again. This procedure was repeated for eight consecutive trials and the averaged values for the last five trials were used to set the DLL.
Paradigm 1: Streaming Paradigm

The streaming paradigm from Snyder et al. (600) was adapted for this study, with the ABA tone triplet sequence customized to tinnitus pitch. The frequency of the A tone was held constant at tinnitus pitch (in controls at the average of tinnitus pitch from tinnitus participants). The frequency of the B tone varied from trial to trial having a frequency difference of 0, 4, 7 and 10 semitones lower than the A tones (hereafter referred to as frequency-0, frequency-4, frequency-7 and frequency-10 conditions respectively). Tone duration was 20ms including 5 ms rise and fall times. The stimulus onset asynchrony was 100ms between adjacent A and B tones within each ABA cycle. The silent duration between ABA triplets was also 100ms. Each trial lasted 10.8 seconds and consisted of 27 repetitions of the pattern. Participants were presented with 80 trials for each frequency condition. Trials were presented in 4 blocks of 80 trials to allow participants to rest between blocks. The first and last repetitions of the ABA pattern within each trial were discarded. The remaining EEG was broken down into epochs of 398 ms (48 ms before and 350ms after the onset of ABA patterns. For time build-up analysis, the 398ms segments were assigned into 5x2s time-bins (corresponding with 5 ABA repetitions per time bin per trial) and averaged resulting in the following time bins: t1, t2, t3, t4, t5. A time window of 160-232ms was used as previous research (600) indicates build-up related activity is reflected within this time period.

The time windows analysed for frequency-related changes corresponded to the B tone N1c waveform (224-292ms) and P2 waveform (252-296 ms); which have been shown to robustly reflect frequency based segregation (600, 604). The regions of interest for ERPs were the left (T7 electrode; N1c time window applied) and right (T8 electrode; N1c) temporal regions, left (FC3; P2) and right (FC4, P2) hemispheric activity and fronto-central (average of Fz, F1, F2, FCz, FC1, FC2, Cz, C1 and C2; P2) regions for traditional montage analysis. Mean amplitude for each group was calculated using arithmetic means over the time windows selected. ERPs were averaged separately for each frequency condition and for each region of interest in the traditional montage analysis.

Paradigm 2: Prediction Paradigm

The prediction stimuli were an isochronous series of tones in which every other tone was a repetition of its predecessor. Omissions were occasionally made (10% of tones) to either the
first tone of a same-frequency tone pair (unpredictable) or to the second tone (predictable). A random omission condition was also included in which single tones were presented and omissions of a tone were occasionally made. Omissions were always made at tinnitus pitch. Tone duration was 50ms including 5 ms rise and fall times with stimulus onset asynchrony of 150ms. For each condition, 1350 stimuli and 150 omissions were presented in one block. The order in which conditions were presented was randomized for each participant. ERPs for tones and omissions were separately averaged for the three conditions. 10-50ms after stimulus onset was the time window used in conjunction with the Bendixen (2009) study as predictive processing should show the strongest effect immediately after expected tone onset (64). Difference waveforms were calculated to control for the effect of context by subtracting ERPs elicited by omissions from those generated by tones presented in the same position – the second tone of the pair for the predictable and first tone of the pair for the unpredictable condition. 10-100ms after onset time windows were used to analyze these tone-omission differences.

8.4.4. Statistical Analysis

Traditional Montage Analysis

For the streaming paradigm, main and interaction effects were examined using a mixed measures ANOVA investigating the effects of group (tinnitus/controls), frequency (frequency-0, frequency-4, frequency-7, frequency-10) and time bin (T1, T2, T3, T4, T5) for following electrode groups: T7, T8, FC3 (left hemispheric activity), FC4 (right hemispheric activity) and average of frontocentral electrodes (F1, F2, FCz, FC1, FC2, Fz, Cz, C1, C2). For prediction, a mixed measures ANOVA was conducted investigating the effects of Group (Tinnitus, Controls) and Condition (Predictable, Unpredictable, Random) for the same electrode groups. For both paradigms, post-hoc Bonferroni tests were used to further compare significant main and interaction effects. Greenhouse-Geisser corrections (if estimate smaller than 0.75) and Huynt-Feldt corrections (if larger than 0.75) were made for violations of sphericity.

sLORETA Analysis

The sLORETA software (R.D. Pascual-Marqui, Key Institute for Brain-Mind Research, Zurich) (605) was used to compute the cortical three-dimensional (3D) distribution of current
density for mean ERPs amplitudes. The sLORETA method is a standardized discrete, 3D distributed, linear, minimum norm inverse solution (605). Thus, sLORETA images represent the standardized electric activity at each voxel in neuroanatomic Montreal Neurological Institute (MNI) space as the exact magnitude of the estimated current density. Anatomical labels are reported using MNI space, with correction to Talairach space. The sLORETA software package was used to perform the statistical comparisons of sLORETA source localization between groups. EEG epochs were imported and processed. Cross spectrums of the ERPs corresponding to the N1c and P2 time windows were obtained for every subject, for the following frequency bands: delta (1.5–6 Hz), theta (6.5–8 Hz), alpha 1 (8.5–10 Hz), alpha 2 (10.5–12 Hz), beta 1 (12.5–18 Hz), beta 2 (18.5–21 Hz), beta 3 (21.5–30 Hz), and gamma (30.5–60 Hz). Independent group t-tests were performed on the generators in order to see if there was a difference between the two groups. Five thousand permutations were used to establish significance levels (p < 0.01) and compute t statistics for the null hypothesis of no difference in activity between tinnitus and control groups (606).

8.5. Results

8.5.1. Streaming Paradigm

Traditional electrode montage analysis: T7 and T8 electrodes

A significant interaction effect between tinnitus and control groups were observed by frequency at the T7 electrode (F(3,45)=4.004, p < 0.05) (Figure 26). For frequency-0 condition, the tinnitus group (M=-0.10, SE = 0.066) had significantly more negative shifts in ERP amplitudes corresponding to the N1c waveform time window than controls (M=0.243, SE = 0.093, F(1,28)=4.944; p < 0.05). There was a marginal difference for frequency-4, with the tinnitus group (M=-0.15, SE=0.068) again showing more negative shifts within the N1c waveform time window than controls (M=0.22, SE=0.096, F(1,28)=3.973; p = 0.056). While the N1c waveform for the control group shifted more negatively with increasing A-B tone frequency differences, the tinnitus group had the reverse trend – N1c amplitudes shifted positively with increasing A-B tone frequency differences.
Figure 26. Mean N1c waveform amplitudes (in microvolts) at the T7 electrode site for the tinnitus (white) and control (black) groups. Solid and dashed lines represent +/- one SE for the tinnitus and control groups respectively. A significant difference in N1c amplitudes was observed between tinnitus and control groups for the frequency-0 condition (indicated with *) and a marginal difference for frequency-4. Significant differences were present within the control group for frequency-0 and frequency-10 conditions (indicated with †). Within the tinnitus group, there were no changes in N1c or P2 waveform amplitudes as a function of frequency. For controls, the frequency-10 (M=-0.063, SE=0.102) condition had a more negative N1c waveform than frequency-0 (M=0.243, SE=0.093, F(3,26)=3.874; p < 0.01). There was no effect of time build-up observed for N1c or P2 amplitudes within and between groups. There were no significant differences observed at T8 by frequency, time or group.

Traditional electrode montage analysis: FC3 electrode

A significant difference between tinnitus and control groups were observed by frequency (F (2.626, 73.528)=3.611, p < 0.01), after a Greenhouse Geisser correction was applied following violation to the assumption of sphericity ($X^2$(77)=131.27, p < 0.001; $\varepsilon=0.548,0.760$) (Figure 27). The tinnitus group (M=0.085, SE=0.041) had more positive shifts in ERP amplitude than controls for frequency-4 (M=-0.048, SE=0.057; p < 0.05); more negative shifts were present for the tinnitus group (M=0.002, SE=0.044) than the control group (M=0.222, SE=0.063; p < 0.01) for frequency-7. This indicated decreased P2 waveforms for frequency-4 and enhanced P2 waveforms for frequency-7 conditions for the tinnitus group compared to controls. Within the tinnitus group, there were no significant
differences in mean amplitudes between frequency conditions. For controls, significantly more positively shifted P2 waveform amplitude was present frequency-7 (M=0.222, SE=0.063) compared to frequency-4 (M=-0.048, SE=0.057; p < 0.05). There was no effect of time build-up observed for mean ERP amplitudes within and between groups.

**Traditional electrode montage analysis: FC4 electrode**

At the FC4 electrode, a significant difference was present between tinnitus and control groups for time (F(3.012, 84.328)=3.383, p < 0.05), after a Greenhouse Geisser correction was applied following violation to the assumption of sphericity (X^2(77)=127.99,p < 0.001;ε =0.519,0.708) (Figure 28). The tinnitus group (M=0.135, SE=0.043) had a more positively shifted P2 waveform amplitude than controls (M=-0.029, SE=0.061; p < 0.05) for T1. There was also a significant difference between tinnitus (M=0.045, SE=0.045) and controls (M=0.214, SE=0.064; p < 0.05) for T3, with the tinnitus group showing a more negatively shifted P2 waveform amplitude. Within the tinnitus group, significant differences were found between T4 (M=0.112, SE=0.038) and T5 (M=-0.098, SE=0.049; p < 0.05). Within the control group, T1 (M=-0.029, SE=0.061) and T3 (M=0.214, SE=0.064; p < 0.05) were significantly different. There was no effect of frequency observed for mean ERP amplitudes within and between groups.

**8.5.2. Prediction Paradigm**

**Traditional electrode montage analysis**

There were no significant differences between tinnitus and control groups in recordings using the prediction paradigm. However, significant differences were observed between individual experimental conditions alone (predictable tone, predictable omission, unpredictable tone, unpredictable omission, random tone, random omission) regardless of participant group.

For the T7 electrode site, predictable omission waveforms (M = 0.967, SE = 0.58) and random omission waveforms (M = 2.2804, SE = 0.8701) had more positive shifts in amplitude than unpredictable tones (M = -0.98, SE = 0.7) (F (5, 28) = 1.131; p < 0.05) (Figure 29). For T8, random omissions (M = 0.9365, SE = 0.4388) were more positively shifted in amplitude than unpredictable tones (M = -1.871, SE = 0.635, p < 0.05); predictable tones (M = 0.2526, SE = 0.3113) were more positively shifted in amplitude than
Figure 27. Mean P2 waveform amplitudes (in microvolts) at the FC3 electrode site for the tinnitus (white) and control (black) groups. Solid and dashed lines represent +/- one SE for the tinnitus and control groups respectively. A significant difference in P2 amplitudes was observed between tinnitus and controls groups for frequency-4 and frequency-7 conditions (indicated with *). Significant differences were present within the control group for frequency-4 and frequency-7 conditions (indicated with ♦).

Figure 28. Mean P2 waveform amplitudes (in microvolts) at the FC4 electrode site for the tinnitus (white) and control (black). Solid and dashed lines represent the SE for the tinnitus and control groups respectively. A significant difference in P2 amplitudes was observed between tinnitus and control groups for T1 and T3 (indicated with *). A significant difference in P2 amplitudes was observed between time-bins T4 and T5 within the tinnitus group (indicated with ♦) and between T1 and T3 within the control group (indicated with ♦).
unpredictable tones (p < 0.05); random tones (M = 0.4037, SE = 0.2435) more positively shifted than unpredictable tones (F(2,28)=1.629, p < 0.05). Predictable omissions (M = 0.42, SE = 1.245) were marginally significantly more positively shifted in amplitude than unpredictable tones (p = 0.057). At FC4, predictable omission waveforms (M = -0.139, SE = 0.2475) were more positively shifted in amplitude than unpredictable tones (M = -1.41, SE = 0.6672) (F (5, 28) = 1.099, p < 0.05).

A.

B.
C.

**Figure 29.** ERP mean amplitudes (in microvolts) (between the 10-50ms time window) at the T7 (A), T8 (B) and FC4 (C) electrode sites for the six different experimental conditions combining tinnitus and control group data. Solid lines represent the SE. Significant differences are indicated with ◆. Error bars represent +/- one standard error.

There was a significant difference in tone-omissions waves for the T7 electrode (F (2, 16) = 2.954, p < 0.001) between predictable (M = 0.648, SE = 0.516) and unpredictable conditions (M = -2.692, SE = 0.622; p < 0.0005), and random (M = -0.136, SE = 0.501) and unpredictable conditions (p = 0.003) (Figure 30).

**Figure 30.** ERP mean amplitudes (in microvolts) (between the 10-100ms time window) at the T7 electrode site for omission-tone experimental conditions combining tinnitus and control group data.
Solid lines represent the SE. Significant differences are indicated with ◆. Error bars represent +/- one standard error.

### 8.5.3. sLORETA analysis

Statistical maps comparing sLORETA solutions between tinnitus and control participants were produced for each experimental condition. For frequency-4 within the N1c time window, statistical maps showed greater cortical sources in the precentral gyrus (frontal lobe, BA = 6, best match = 2mm) for tinnitus participants than for controls, and lower sources in the superior frontal gyrus (frontal lobe, BA = 11, best match = 1mm), middle frontal gyrus (frontal lobe, BA = 8, best match = 1mm), inferior frontal gyrus (frontal lobe, BA = 47, best match = 2mm), parahippocampal gyrus (limbic lobe, BA = 35/36, best match = 1mm), fusiform gyrus (occipital lobe, BA = 19, best match = 3mm), right insula (Sub-lobar, BA = 13, best match = 2mm) and right superior temporal gyrus (temporal lobe, BA = 22, best match = 2mm) for tinnitus than for controls (Figure 31).

For frequency-7 within the N1c time window, analyses showed greater cortical sources in the superior frontal gyrus (frontal lobe, BE = 8, best match = 5mm), left superior middle frontal gyrus (frontal lobe, BA = 6, best match = 3mm), precentral gyrus (frontal lobe, BA = 6, best match = 4mm) and superior parietal lobule (parietal lobe, BA = 7, best match = 2mm) for tinnitus participants than for controls (Figure 32). Lower sources in the right superior temporal gyrus (temporal lobe, BA = 38, best match=2mm), insula (sub-lobar, BA = 13, best match = 1mm), inferior frontal gyrus (frontal lobe, BA=45, best match=2mm), anterior cingulate (limbic lobe, BA = 32, best match = 1mm), regions of the middle frontal gyrus (frontal lobe, BA = 9, best match = 2mm), cingulate gyrus (limbic lobe, BA = 23, best match = 1mm) and posterior cingulate (limbic lobe, BA = 29, best match = 2mm) were present for tinnitus participants than for controls.

For the frequency-7 condition within the P2 time window, greater cortical sources were present in the precentral gyrus (frontal lobe, BA = 6, best match = 2mm) for tinnitus participants than for controls (Figure 33). The only statistical difference in oscillatory rhythms between tinnitus and control groups was for the frequency-7 condition, where significantly lower beta-2 activity was observed in sources corresponding to the right inferior occipital gyrus of the occipital lobe (BA 19, best match=1mm) for tinnitus compared to
controls (Figure 34). There was no difference in oscillatory band activity between predictable, unpredictable or random omission-tone conditions.

**Figure 31.** Grand average of the statistical maps comparing oscillatory band activity between tinnitus sufferers and controls for the frequency-4 condition (N1c time window). The brighter colours indicate higher values of the t-statistic according to the colour scale. Blue indicates regions which show greater activation in the tinnitus group compared to controls; red indicates regions with greater activation in controls compared to the tinnitus group. Analysis showed significant greater cortical sources in the precentral gyrus (BA = 6) for the tinnitus group than controls and lower sources in the superior frontal gyrus (BA = 11), middle frontal gyrus (BA = 8), inferior frontal gyrus (BA = 47), parahippocampal gyrus (BA = 35/36), fusiform gyrus (BA = 19), right insula (BA = 13) and right superior temporal gyrus (BA = 22).
Figure 32. Grand averages of the statistical maps comparing oscillatory band activity between tinnitus sufferers and controls for the frequency-7 condition (N1c time window). The brighter colours indicate higher values of the t-statistic according to the colour scale. Two views are provided to highlight sources at different planes. Blue indicates regions which show greater activation in the tinnitus group compared to controls; red indicates regions with greater activation in controls compared to the tinnitus group. Analyses showed greater cortical sources in the superior frontal gyrus (BE = 8), left superior middle frontal gyrus (BA = 6), precentral gyrus (BA = 6) and superior parietal lobule (BA = 7) for the tinnitus group than controls and lower sources in the right superior temporal gyrus (BA = 38), insula (BA = 13), inferior frontal gyrus (BA = 45), anterior cingulate (BA = 32), regions of the middle frontal gyrus (BA = 9), cingulate gyrus (BA = 23) and posterior cingulate (BA = 29/30).

Figure 33. Grand averages of the statistical maps comparing oscillatory band activity between tinnitus sufferers and controls for the frequency-7 condition (P2 time window). The brighter colours indicate higher values of the t-statistic according to the colour scale. Blue indicates regions which show greater activation in the tinnitus group compared to controls; red indicates regions with greater
activation in controls compared to the tinnitus group. Analyses showed greater cortical sources in the precentral gyrus (BA = 6) for the tinnitus group than controls.

**Figure 34.** Grand average of the statistical maps comparing oscillatory band activity between tinnitus sufferers and controls for the frequency-7 condition. The brighter colours indicate higher values of the t-statistic according to the colour scale. Analysis showed significant lower sources of beta-2 (18.5–21 Hz) rhythms in the right inferior occipital gyrus (BA 19) in the tinnitus group.

**8.6. Discussion**

This study investigated the possibility of different auditory streaming and predictive processing between individuals with tinnitus and controls (with hearing loss but no tinnitus). EEG was used to examine brain electrical activity difference, as an indirect measure of potential underlying cognitive processing and cortical source differences.

**8.6.1. Streaming Paradigm**

Our results showed an unusually greater N1c waveform upon B tone onset among tinnitus participants in the absence of any tone deviation (frequency-0 condition) at the left primary auditory cortex (lateral superior temporal gyrus) (276) region. A significant larger N1c waveform for the frequency-10 than frequency-0 condition was observed in the control group; however, there were no differences between conditions for the tinnitus group. Hemispheric differences were present with the tinnitus group having significantly reduced frequency-4 and enhanced frequency-7 P2 waveforms than controls within the left frontal
hemisphere only. In the right frontal hemisphere, P2 waveform differences were observed between certain time bins (T1 and T3). No differences between the two groups were found at the frontocentral sites.

In the frequency-4 condition in the N1c time window, there was significantly less activity localized to frontal regions (superior/middle/inferior frontal gyrus) and superior temporal gyrus for tinnitus participants compared to controls as computed with sLORETA. Other regions with significantly relatively reduced activity included the parahippocampus, insula and fusiform gyrus. The precentral gyrus had greater activity in tinnitus participants than controls. In contrast, for frequency-7 for the N1c time window, there was greater superior frontal gyrus, middle frontal gyrus, precentral gyrus and superior parietal lobule activity for tinnitus. Lowered activity was present in the right superior temporal gyrus, insula, inferior frontal gyrus, anterior cingulate, regions of the middle frontal gyrus, cingulate gyrus and posterior cingulate. For the P2 time window for frequency-7, greater activity was observed in tinnitus for the precentral gyrus than for controls.

**Disruption to Streaming**

The N1c is proposed to reflect the directing of selective attention towards stimuli (260) as well play a role in temporary memory storage of information (61). A minimal N1c waveform is theoretically expected for the frequency-0 condition as there is no deviance present in frequency between the onset of the first (A) tone and second (B) tone. Individuals with tinnitus display a robust effect of reduced formal working memory and attention performance compared to non-tinnitus individuals (159, 183, 607, 608) as well as more global deficits in cognitive processing (609). Under the general depletion of resources theory (335), this can be modelled as that cognitive resources are directed towards the tinnitus signal, therefore there is less cognitive reserve for performing tasks which require voluntary, conscious, effortful, and strategic control (182). It is possible that the presence of tinnitus continuously occupies temporary memory storage and, under the prediction error hypothesis, the cortex is constantly processing prediction error arising from tinnitus. Schroger et al. (2015) have similarly proposed that attention and prediction are interdependent, based on predictive models in which predictions are sent from higher-order regions to lower level sensory areas, while attention modulates the feedforward process of prediction error to higher-order regions (297). This latter bottom-up process may be adjusted voluntarily, based on intention of the listener.
An enhanced resting-state N1c waveform is always generated as a result, and in this case, this is also plausible given that the frequency-0 condition presents a B tone matched to each individual’s tinnitus. As frequency differences increases, global cognitive resources are recruited for making coherence/segregation perceptual judgments in streaming, and this significant difference would gradually disappear. In this study there were no differences in N1c waveforms between tinnitus and control participants for the right primary auditory cortex, which is discrepant with previous findings of generally enhanced right hemisphere N1c activity (272, 276, 610).

It was of interest that in the control group, normal growth in N1c responses was observed as frequency differences increased between tones A and B. However, the tinnitus group did not show this effect – in fact, although not statistically significant, there appeared to be a general decrease in N1c over increases in the frequency of deviant stimuli. Within the ambiguous region of stream segregation processing, attention or contextual alterations can bias perception towards either coherence or streaming (597). In visual models of perceptual bistability, the process of selecting one percept is similar to prediction error adaptation, whereby there is gradual neural suppression at the level of thalamocortical synapses of the percept that is not attended to (61, 611). Tinnitus is present as another percept which is in competition within the other two tone streams; moreover, it is preferentially processed by the auditory system due to the salient and discrepant characteristics conflicting with expectations of a real sound. Also selective attention mechanisms are thought to suppress qualitatively similar unattended stimuli during streaming (612), as would be the case of A and B tones in relation to tinnitus (often tonal in nature) (34) as well as reduce cognitive reserve remaining for making and/or altering perceptual bias streaming judgements. The nature of disruption potentially elicited by tinnitus cannot be fully understood based on this study alone and further studies are needed expanding on this preliminary examination.

Modelled under the Adaptation Level Theory (ALT) framework (6), high prediction errors generated by tinnitus will increase the weighting placed on tinnitus and residual components (via shifts in attention). As a result, tinnitus magnitude and perceptual dominance is increased. The decreased weighting on external sound components will reduce resources allocated to processing incoming auditory input, increasing the difficulty in decoding and understanding external sound.
There is a good body of research to suggest that the presence of tinnitus (above any hearing loss) reduces speech discrimination in everyday situations (165, 613-615). Disruption to auditory streaming may at least partially explain this effect as the ability to separating out different sound source, especially in noisy situations (e.g. following a stream of conversation in cafes/restaurants) relies on accurate stream segregation. Errors in simultaneous grouping results in blending of sounds that should be heard as separate (591), and this blending can distort characteristics (e.g. frequency, quality or timbre) of incoming sounds.

**Source Localization**

The regions with contrasting activity between tinnitus and controls identified in this study overlap considerably with the resting state (in quiet, no task administered) functional connectivity networks of tinnitus: regions of the limbic system, auditory system, default mode network (DMN), attention (dorsal attention network (DAN), ventral attention network (VAN), executive networks of attention) and visual networks (313, 314, 477).

The precentral gyrus forms part of the DAN, which plays a role in orienting attention to a particular task (616) and may receive goal-directed, top-down feedback (617). The increase in precentral gyrus activity among tinnitus participants for intermediate frequency conditions for N1c as well as P2 might indicate greater levels of top-down attention recruited to carry out streaming and segregation under conditions of perceptual uncertainty, due to the extra attention recruited by tinnitus. Decreases in right superior temporal gyrus (part of the VAN which responds to external stimuli, is more dominant in the right hemisphere and which is generally activated for unexpected diversion of attention away from a task (312)) and decreases in insula, middle and inferior frontal gyrus regions (part of executive, purposeful control of attention) can suggest disruption to sensory processing of external stimuli, potentially due to limitations imposed on working memory capacity by the simultaneous presence of tinnitus signals.

Schmidt et al. (2013), found increased resting-state connectivity between right parahippocampus and dorsal attention network for tinnitus (477). This increase could be a compensatory attempt to manage the phantom sound, delegating that process to non-attention processing regions such as the limbic system (464, 474). Regions of the parahippocampus and insula that showed decreased activation in tinnitus compared to controls for this study might be because it is processing tinnitus as opposed to the streaming sound stimuli.
However, it is important to note that other studies looking at the DAN and tinnitus have not found any connectivity differences with other regions (312, 618).

**Interpretation of findings: Hemispheric differences and time build-up**

In our study, differences were observed within the frontal cortex by hemisphere. The P2 component reflects similar underlying cognitive processing to that of the N1c (272) and the amplitude increases with memory load (277). It may have multi-site generators in the cortex, localizing predominantly to the vertex, with considerable primary and secondary auditory cortices involvement as well. The tinnitus group had significantly reduced frequency-4 and enhanced frequency-7 P2 waveforms than controls within the left hemisphere. For the right frontal hemisphere, significant differences were present by time such that the tinnitus group had a lower P2 in the first time bin (T1) and a higher P2 in the later T3 time bin compared to controls. Within the tinnitus group, the last time bin (T5) had significantly lower P2 than the previous bin (T4). In the control group, T1 had significantly lower P2 waveforms than T3. These results are difficult to interpret as time build-up is complex. Streaming takes several seconds to build-up and is influenced by top-down control (339). Any biasing effect (such as attentional diversion by tinnitus) which might increase or decrease coherence or segregation can reset build-up and also remains for several seconds (339). However, the results do indicate that frequency and time aspects of streaming may be processed by different hemispheric regions of the cortex and within each hemisphere, and subtle changes in streaming processing are present in conjunction with the presence of tinnitus in an individual.

**8.6.2. Prediction Paradigm**

For the predictive paradigm, the 10-50 ms time window following stimulus onset was used as sequential predictive coding processes tend to exhibit the strongest effect immediately after expected tone onset (61, 64). Tone-omission waveforms were also calculated to remove the effect of context potentially provided by preceding tones (as well as late ERP influences).

There was no support for our hypothesis of differences in processing tones and omissions within the predictive paradigm for tinnitus and controls. As a group (tinnitus and controls together), for the left primary auditory cortex, tone-omission difference waveforms, significant differences were observed between unpredictable and predictable conditions, as
well as between unpredictable and random conditions. The difference waveform for unpredictable was a greater negative deflection. Random difference waveforms were also negative-going but of lower magnitude, and the predictable waveform was positively deflected. This finding is similar to that observed in Bendixen et al. (64) for tone-omission waveforms, whereby the predictable condition resulted in a more positive-going waveform than random and unpredictable condition difference ERPs. As the auditory system actively generates predictions, cortical memory representations of sounds are activated in expectation before the arrival of the second sound – this is what is observed for the predictable condition paradigm (thus an omission of the second tone results in similar ERPs to if the tone was actually presented). However, when the omissions are unpredictable or random, this is treated as a deviance. Some significant differences were present between individual experimental conditions for the left and right primary auditory cortex and the right frontal hemisphere, but they were between unrelated conditions (e.g. unpredictable tones and predictable tones, which are both the first tones of the pairs) that do not have a justifiable relationship within a prediction error framework. These results contrast with Bendixen et al. (64) which involved normal hearing participants and where there was observed significant differences between unpredictable tones and omissions and random tones and omissions. It is not known if the differences arise due to the presence of hearing loss among participants in this study.

**Thalamocortical Dysrhythmia Theory**

The results of this study do not support the Thalamocortical Dysrhythmia hypothesis of greater theta and gamma activity between tinnitus participants compared to controls. Only for the frequency-7 condition was there was significantly lower beta-2 band activity present for tinnitus, correlating most within the right inferior occipital gyrus. Given the multiple comparisons included in the analysis, it is acknowledged by the authors that it is possible to observe a significant effect by chance. The findings support the conclusions reached by other review studies (573, 603) of mixed empirical findings of oscillatory activity differences with tinnitus. A key reason for this might be the different paradigms under which tinnitus and controls are compared (e.g. a difference was observed with ABA streaming paradigm but not omission-tone paradigm in our study). With regards to beta band activity (12-30 Hz), various studies have reported either null effects with regards to oscillatory changes (566-568) (292, 549, 569) or tinnitus-related effect (144, 571) (562, 619). It is possible for the differences to arise based on participant inclusion and exclusion criteria. Beta oscillations are involved in
top-down signaling and also presumably control lower-level gamma activity (552). The reduction in beta oscillatory activity, in conjunction with reduced superior temporal gyrus and certain frontal region activity for tinnitus participants in the intermediate frequency difference conditions may suggest that the deviance introduced by the B tone is not resulting in top-down predictive feedback, therefore there is disruption or discontinuation of streaming processing higher up in the cortical regions.

**General Limitations**

While the two groups were matched for hearing loss (no significant difference), subtle differences in hearing thresholds between groups acting as potential confounders cannot be completely excluded in this study. Audiometric thresholds can affect auditory streaming results, however, aging exclusively does not appear to have an effect (594, 604). While the tinnitus group had tinnitus pitch set individually based on psychoacoustic matching the control group had the ‘tinnitus pitch’ set using the mean tinnitus pitch value of the tinnitus group. Therefore, it is possible for this frequency to fall outside of the regions of deafferentation for some participants. Memory and learning processes may further drive functional connectivity alterations in intrinsic tinnitus networks between auditory networks, visual network, limbic networks, and attentional networks (313). Structures which are implicated in this are the: amygdala, the hippocampus (memory-based learning) and the parahippocampal area (memory recollection) (4). Due to the limited spatial resolution provided by EEG, it is acknowledged that there are drawbacks in accurately discerning subcortical structures which might be differentially involved in streaming and prediction between tinnitus and control groups.

**8.7. Conclusions**

The findings from this study imply that cortical-level frequency-based auditory stream segregation is disrupted among individuals with tinnitus at or near the frequencies corresponding to tinnitus pitch, observed as enhanced resting-state N1c and abnormal growth of N1c waveforms across conditions. Disruption may occur within the ambiguous streaming region, in which attention or contextual alterations can bias perception towards either coherence or streaming. In such instances, topographically-restricted prediction errors continually generated in tinnitus, along with top-down feedback, tinnitus salient characteristics and conflict with expectations of sound can lead to tinnitus recruiting attention
and cognitive resources during the later stages of object processing. As a result, streaming processing of external tones in the ABA paradigm may be compromised. There were different levels of activity between tinnitus and control groups in regions corresponding to attentional networks (precentral gyrus, right superior temporal, insula, middle and inferior frontal gyrus) as well as limbic regions (parahippocampus and insula). Under the ALT framework, attention is increased towards, which increases tinnitus AL. This increase is greater than any bias towards shifts in AL for the external sound played. There was no support in this study for differences in theta and gamma activity between tinnitus and controls. A reduction in beta-2 oscillatory activity was observed for the tinnitus group in conjunction with reduced superior temporal gyrus and certain frontal region activity for intermediate frequency conditions. Beta band activity is hypothesized to be involved in top-down predictive feedback, which might be compromised higher up in the cortical regions following streaming disruption; however this is difficult to conclude as a result of discrepancies in current literature. Within the context of everyday life, streaming difficulties among tinnitus sufferers can translate into difficulties in separating out different sound sources in noisy situations (e.g. following a stream of conversation in noisy environments). Errors in simultaneous grouping results in blending of sounds that should be heard as separate, and this blending can distort characteristics (e.g. frequency, quality or timbre) of incoming sounds. It would therefore be useful clinically to provide additional counselling and/or teach individuals with tinnitus strategies for coping with hearing in complex environments, similar to techniques taught for hearing loss, such as facing the person, reducing distance between speaker and themselves, etc. Further research based on compiling EEG data from various studies (i.e. compiling large-scale databases) and applying standard protocols may enable for a clearer understanding of neural oscillatory changes in tinnitus.

In conclusion, this study supports models of tinnitus in which tinnitus is initially processed as an auditory object (5, 6) but disruption related to auditory streaming occurs in the later stages. Topographically-restricted prediction errors may be continually generated as a result (7). This may indirectly disrupt streaming and analysis of external sound by depleting attentional resources. There was no support for the Thalamocortical Dysrhythmia hypothesis of greater theta and gamma activity between tinnitus participants compared to controls.
Chapter 9. A clinical trial of Broad Band Noise and Nature sounds for tinnitus therapy: Group and individual responses modelled under the Adaptation Level Theory of Tinnitus.
9.1. Preface

Publication

This chapter includes content from the article “A clinical trial of Broad Band Noise and Nature sounds for tinnitus therapy: Group and individual responses modelled under the Adaptation Level Theory of Tinnitus” submitted for publication in Frontiers in Aging Neuroscience.

What was undertaken?

A randomized clinical trial was conducted comparing the effectiveness of nature sounds with broadband noise. The primary outcome measure was tinnitus impact on life, measured using total TFI scores. A variety of other experimental outcomes related to tinnitus (loudness and annoyance ratings, loudness level matches, minimum masking levels), positive and negative emotionality, attention (attention reaction time and discrimination time) and psychological state (anxiety, depression, stress) were also measured. A randomized cross-over design was employed. Each sound was administered for 8 continuous weeks, with a 3 week wash-out period in between sound conditions. Measurements were taken at sound fitting, 4 weeks after administration and 8 weeks after administration. Qualitative interviews were conducted at each time point of the trial.

The administration of sound therapy led to an overall reduction in tinnitus impact of life over 8 weeks; the presence of sound also resulted in small but significant changes in secondary outcome measures of tinnitus and general psychological affect. Broadband noise resulted in significantly greater reduction of tinnitus impact of life than nature sounds. There was a significant effect of intervention on tinnitus loudness level matching; an increase in level of external sound needed to match tinnitus was observed between baseline and 8 weeks follow-up for BBN, while there was a slight decrease in loudness level matches for nature sound between baseline and 8 weeks follow-up. Individual variability in response to sound therapy was present.

Why was this needed?

A successful sound is not one that affects tinnitus alone, but should be comfortable as well. Despite its popularity, there is no consensus as to the most appropriate sound parameters for
tinnitus sound therapy, or if the treatment provides independent benefit over psychological effects alone. Testing different parameters and individual preferences of sound therapy are therefore significant in strengthening support for and improving its clinical effectiveness. The presence of several influencing factors on tinnitus-external sound interactions (residuals) might account for individual success (or lack of success) with sound therapy. Currently, the selection of sound type based on individual needs does not appear to be widespread or documented in sound therapy. For this study, it was of interest to administer a randomized control trial to investigate a novel parameter of dynamic sound which may influence tinnitus: predictability. This study incorporated findings of the emotion experiment discussed in Chapter 5, narrative review of Chapter 6 and adaptation experiment and feasibility trial discussed in Chapter 7 in designing sound therapy stimuli and controlled for personality trait influences.

How does it contribute to the objectives of the PhD?

This study incorporated the various ALT residuals of personality traits, emotion, memory and prediction as well as attention into its design. By measuring multiple residuals at different time points, it was possible to examine the contributory effects of and map changes in each residual over time. In this study, the presence of external sound in general resulted in improved tinnitus outcomes. Interpreted under an ALT framework, internal AL weighting shifts directly away from the tinnitus signal and towards the sound therapy stimuli can occur over time. However, another indirect tinnitus-residual-external sound pathway may also exist by which tinnitus is alleviated as a result of psychological relief, potentially involving complex non-auditory networks. Predictable sounds may undergo loudness adaptation at a faster rate, such that tinnitus AL shifts are prevented and/or result in shifts back towards tinnitus earlier than for Unpredictable sounds. Our study findings support that use of tinnitus loudness level match changes as a long-term intervention measure is complicated by the fact that sound stimuli undergo loudness adaptation as well (shifts in external sound AL), and this can occur to a greater extent than tinnitus adaptation (shifts in tinnitus AL). Measuring tinnitus magnitude (encompassing various higher-order psychosocial factors and combining attributes of loudness, severity and tinnitus awareness) may be a more realistic estimate of intervention outcome than psychoacoustic matches alone.
9.2. Abstract

Objectives: A randomized cross-over trial in 18 participants tested the hypothesis that nature sounds, with unpredictable temporal characteristics and high valence would yield greater improvement in tinnitus than constant, emotionally neutral broadband noise.

Study Design: This study was a mixed methods cross-over trial. The primary outcome measure was the Tinnitus Functional Index (TFI) (110). Secondary measures were: loudness and annoyance ratings, loudness level matches, minimum masking levels, impact on life, positive and negative emotionality, attention reaction and discrimination time, anxiety, depression and stress. Each sound was administered using MP3 players with earbuds for 8 continuous weeks, with a 3 week wash-out period before crossing over to the other treatment sound. Measurements were undertaken for each arm at sound fitting, 4 and 8 weeks after administration. Qualitative interviews were conducted at each of these appointments.

Results: From a baseline TFI score of 41.3, sound therapy resulted in TFI scores at 8 weeks of 35.6; broadband noise resulted in significantly greater reduction (8.2 points) after 8 weeks of sound therapy use than nature sounds (3.2 points). The positive effect of sound on tinnitus was supported by secondary outcome measures of tinnitus, emotion, attention and psychological state, but not interviews. Tinnitus loudness level match was higher for BBN at 8 weeks; while there was little change in loudness level matches for nature sounds. There was no change in minimum masking levels following sound therapy administration. Self-reported preference for one sound over another did not correlate with changes in tinnitus.

Conclusions: Modelled under an adaptation level theory framework of tinnitus perception, the results indicate that the introduction of broadband noise shifts internal adaptation level weighting of the tinnitus signal, reducing tinnitus magnitude. Nature sounds may modify the affective components of tinnitus via a secondary, residual pathway, but this appears to be less important for sound effectiveness. The different rates of adaptation to broadband noise and nature sound by the auditory system may explain the different tinnitus loudness level matches. In addition to group effects there also appears to be a great deal of individual variation. A sound therapy framework based on adaptation level theory is proposed that accounts for individual variation in preference and response to sound.
Subjective tinnitus is the involuntary perception of one or more sounds by an individual, in the absence of an external physical source (1-4). It is now broadly understood to arise as a result of peripheral lesions in the auditory system resulting in altered cortical input. This triggers compensatory neuroplasticity changes across several overlapping brain networks (9, 79, 160, 313, 620). Final tinnitus magnitude is thought to result from activity within auditory, personality, emotion, attention and memory networks (5, 6, 10). Fifteen-20% of the tinnitus population experience significant disruption to quality of life (11, 12), manifesting as impaired concentration, problems with hearing, irritation, frustration and annoyance, anxiety, depression, disruption of everyday activities and disturbed sleep (13, 84, 87, 93, 103).

Reports of tinnitus affect vary a great deal from individual to individual, leading to models of tinnitus that include individual psychology and personality as strong contributors (5, 6). A failure to account for the homogeneous nature of tinnitus has likely contributed to the difficulties in identifying useful therapies.

Sound therapy is currently widely used in several tinnitus treatment paradigms. Sound therapy uses external sounds to modify tinnitus perception and/or reactions to it (5, 20-24). Immediate effects are provided by masking (20, 21), and long-term changes in tinnitus functional networks have also been observed (25-27). The potential for tinnitus and external sound to interact exists as both undergo similar auditory processing within the system, including feature extraction, schema formation and semantic objective formation (5, 6). Although categorization of patient characteristics has been used to guide focus of treatments (e.g. hearing aids, counselling, use of sound therapy (33)), the selection of sound type based on individual needs does not appear to be widespread or documented. Sounds used in therapy include broad-band noise (BBN), narrow-band noise (either pitch-matched or unmatched to tinnitus), nature sounds or music (28-30). Despite its popularity, there is no consensus as to the most appropriate sound parameters for tinnitus therapy, or if the treatment provides independent benefit over psychological effects (20, 31, 32) or hearing aids (621). Several recent studies using different types of sound have shown small (213) or no significant differences in effect (622) of different therapy sounds on tinnitus. There is some evidence that dynamic sounds that temporally vary may provide greater benefit for reducing tinnitus symptoms compared to fixed intensity sounds (29, 582-584). Customized music and
counseling applied via the Neuromonics Tinnitus Treatment for six months resulted in greater alleviation of tinnitus symptoms and greater user acceptability than when participants were provided with counseling and BBN, or counseling only (216). Schreitmüller et al. (2013) observed that nature sounds, even though they presented with higher dynamics and higher masking thresholds, were accepted more by the listener than white noise (220). Ocean or wave sounds have recently been introduced by several hearing aid manufacturers in their tinnitus therapy devices (221, 222).

The reasons why temporally varying sound may be more effective in treating tinnitus in some individuals are unclear. The added therapeutic success of dynamic sounds, particularly sounds relevant to an individual’s everyday environment, may be due to the provision of greater informational (central) auditory masking, whereby both therapeutic sound and tinnitus compete for cognitive resources (171). Informational or “central” masking is possible with tinnitus as the phenomenon is due to central processing itself. Another way in which music or nature sounds can promote relief is by engaging the emotional regions of the brain; as relaxation aids tinnitus habituation (216, 217). Unpleasant sounds mimicking tinnitus have been found to activate the tinnitus network more strongly than neutral tones {Schlee, 2008 #164}. Simulation of tinnitus (using an aversive tinnitus-like auditory stimuli) in patients without tinnitus has been shown to activate neural networks comparable to that of tinnitus, including recruitment of the limbic system {Mirz, 2000 #557; Mirz, 2000 #545}. Differences in processing of pleasant sounds have also been observed between tinnitus patients compared to those without hearing loss or tinnitus {Carpenter-Thompson, 2014 #555}, as greater activation of the bilateral hippocampus and right insula. It is possible that tinnitus and emotionally negative auditory perceptions from known sources may share similar neural processing networks, which are counteracted by the presence of pleasant stimuli. Short term exposure to emotional stimuli in the auditory modality (but not visual modality) influences ratings of tinnitus: with presentation of more unpleasant sounds resulting in increased tinnitus magnitude (623).

An alternative or complementary mechanism for possible advantages of dynamic sound relates to their predictability. Prediction and expectation are integral to human survival. At each level of the sensory processing hierarchy, incoming sensory input is combined with existing internal memory representations to generate predictions (497, 575, 576). The formation of predictions operates independent of attention and relies on Gestalt principles of
perception (574) as well as top-down Bayesian processes (497) (61, 68-70). Only prediction error, the difference between the two templates (such as that generated by novel signals) is enhanced and encoded further. The internal memory representation is also updated top-down in order to alter the receptive field properties of low-level sensory units for future events (489). According to De Ridder et al. (7), peripheral deafferentation and missing auditory input generates topographically-restricted prediction error. Subsequent central plasticity processes then attempt to ‘fill in’ for this prediction error, resulting in neuronal hyperactivity (2, 577), synchronized neural activity (578, 579), cortical map changes (96, 113) and aided memory retrieval (4), ultimately giving rise to the sensation of tinnitus. A shift in cognitive focus to process tinnitus prediction error might also elicit competition for brain reserve to process external deviant sounds. Alterations in predictive sound processing may exist amongst tinnitus sufferers compared to controls, persons with tinnitus may have: heightened gamma band activity (67, 145), differences in deviance detection (237, 559), and reduced performance in working memory and attention tasks (183, 624). Although trends in these relationships occur, there is often a high degree of variation, which likely reflects the multifactorial effect of tinnitus within individuals and the influence of the individual, and environment, on tinnitus (5, 6).

The adaptation level theory (ALT) model of tinnitus predicts that BBN and sounds that fluctuate or are emotive (such as nature sounds in our soundscape) should both affect tinnitus positively but through different mechanisms. Variables affecting the success of different sounds might include an individual-specific top-down processing related to personality, memory, prediction, attention and emotion as well as bottom up processes related to primitive auditory analysis such as contrast (5). Up until this study there have been no controlled trials to test sound therapy based on ALT. The presence of several influencing factors on tinnitus-external sound interactions might account for individual success (or lack of success) with sound therapy. A successful sound therapy is not one that affects tinnitus alone; it must be comfortable as well. Testing different parameters and individual preferences of sound therapy are therefore significant in strengthening support for, and improving, sound therapy effectiveness (625).

We hypothesized that nature sounds, would affect top-down processing, possibly eliciting prediction errors to compete with tinnitus, and this, along with positive effects on emotion would result in greater reduction in tinnitus magnitude than BBN, that would primarily affect
Barozzi et al. (622) found that nature and BBN resulted in similar reductions of the Tinnitus Handicap Questionnaire (THQ) following six months of administration, but they did not explore individual characteristics and mechanism of benefit relative to study outcomes. An experimental study piloting some of the methods employed here (626) found that 30 minutes administration of unpredictable surf-like sound resulted in significantly lower tinnitus loudness than a predictable surf sound. A two week feasibility trial found greater number of participants preferred the unpredictable surf sound. The effects of other contributory factors (e.g. greater relaxation to one sound over the other, different emotions evoked by the two sounds, anticipation) were not controlled for in that short-term trial. A longer-term clinical trial comparing BBN and nature sounds measuring various individual residuals (e.g. emotion, attention) was deemed critical to understand sound therapy effects.

9.4. Methods

This study was approved by the University of Auckland Human Participants Ethics Committee. All subjects gave written informed consent in accordance with the Declaration of Helsinki. This trial was registered on Australian New Zealand Clinical Trials Registry (ANZCTR) (Trial #12616000742471).

9.4.1. Recruitment

The inclusion criteria were: adults aged between 18-69 years residing in the Auckland region (NZ), constant tinnitus and a minimum weighted score of 21 on the Tinnitus Functional Index (TFI) (this cut-off score is calculated based on convergent validity results between TFI mean scores and response levels of a tinnitus global severity item; a score of 21 delineates individuals who consider their tinnitus as problematic from those who do not view tinnitus as a problem) (110), normal middle ear function, and a maximum of a moderate degree of hearing loss (less than 70 dB loss on average across the frequency range of 125-8000 Hz). A participant information sheet was provided to participants that outlined the background and aims of the trial and details of measurements to be taken at various appointments.
9.4.2. Participants

A power analysis indicated that 21 participants would need to enter this two-treatment crossover study. The probability was 80 percent that the study will detect a treatment difference at a two-sided 0.05 significance level, if the true difference between treatments was 13.0 units on the TFI. This is based on the assumption that the standard deviation of the difference in the TFI is 20 (110, 627).

Twenty-five participants (8 females, 17 males, mean age=56.31, range 37-65) from the University of Auckland Tinnitus Research Volunteer Database met the inclusion criteria and were recruited. Six participants did not meet the criteria and were excluded. Nineteen participants (7 female, 12 male, mean age=60.63, range 38-65) completed the trial, retention was 76%. Six participants were lost to follow-up (did not respond to emails, attend follow-up appointments and/or did not finish trialling both sounds). In such cases, the data was not usable. Early termination of trial refers to cases where participants voluntarily expressed they wanted to stop the trial between the 4 week and 8 week appointment period for one or both of the Intervention sounds, but still attended follow-up appointments.

The mean Tinnitus Functional Index (TFI) score of participants was 44.4 (SD=17.33). All participants had experienced chronic bothersome tinnitus for a minimum of 4 years with an average length of time since tinnitus onset of 17 years (SD=11.94, ranging from 4 - 45 years). Forty-two percent of participants described tinnitus quality as cricket sounds, 37% as tonal and 21% as noise. Measured tinnitus pitch ranged from 800Hz to 15750 Hz in participants, and there was no clustering observed around any particular pitch match. Sixty-eight percent of participants had not used any form of tinnitus treatment in the past, 16% had tried one treatment and 16% had tried more than one treatment. Three out of the 19 participants (16%) wore hearing aids; all of them wore bilateral aids. When asked whether loud sounds tended to make their tinnitus worse, 42% responded that it did exacerbate it, 32% responded no and 26% did not know. Forty-two percent of participants felt that their tinnitus was reduced by music or by certain types of nature sounds (such as the noise of a waterfall, running shower water, etc.) and the remaining 58% did not know.
9.4.3. Materials and Tests

9.4.3.1. Sound Therapy Stimuli

Broadband noise (BBN) was generated by Audacity 2.1.2. (628). The natural sounds were Surf, Cicadas/Farm Sounds and Rain sounds directly recorded from the natural setting by the

A

B
Figure 35. Unweighted power spectrum density plots (dB SPL/Hz) showing relative signal strength across frequencies using an artificial ear for the three nature sounds used in the study for Unpredictable sound therapy (Surf (A), Cicadas/Farm Sounds (B), Rain (C)) and BBN for Predictable sound therapy (D). A G.R.A.S. Artificial Ear Type 43AC coupler was used and sounds were played directly through the MP3 and Panasonic earphones. Recordings used a National Instruments PXI-4461 sound card and LabVIEW 8.0 was used to analyse the sounds.

Researchers using a Roland R-05 WAV/MP3 Recorder with CS-10 EM binaural ear level microphones and edited to 30 minutes duration using Audacity 2.1.2. software (628). All stimuli were adjusted for sound level such that the long-term average loudness (dB SPL) was equivalent. The frequency spectra of the stimuli developed for this study are displayed in Figure 35.
9.4.3.2. Tinnitus loudness and annoyance functions and Selection of Nature Sound

BBN and the three nature sounds were played for two minutes each (in randomized order) at the participants desired comfort level. At the end of each sound, participants were asked to rate the sound on a scale of 1-10, with 1 corresponding to a highly negative and/or unpleasant sound and 10 corresponding to highly positive and/or pleasant sound.

BBN and the three nature sounds again were played (in randomized order) to participants at increasing sound levels: from the threshold at which the sound was first heard to the minimum masking level (MML) where the sound first masked the individual’s tinnitus. Tinnitus annoyance and Tinnitus loudness ratings (on a scale of low 0-10 high) were undertaken at fixed sound level intervals from 0 dB SL to MML. Participants were also asked to judge the relative loudness of tinnitus and noise on a scale of 1-10 as each sound was increased in sound level, with 0 corresponding with the nature noise being not audible (tinnitus is only audible) and 10 being tinnitus is not audible (fully masked by the sound).

At the end of the task, participants were asked to select which nature sound they preferred to use for tinnitus treatment, and asked the following questions:

1. Why did you select this particular sound?
2. What kind of feelings (if any) does this sound elicit?

The average valence rating, Equal loudness Level (the sound level where the combined tinnitus and noise loudness rating given to a noise level is 5, indicating that both tinnitus and noise are of equal perceived loudness) and Equal Annoyance Level (the sound level tinnitus annoyance rating functions and noise annoyance rating functions intersect, indicating that both tinnitus and noise are of equal perceived annoyance) of all participants were calculated and recorded for BBN and each environmental sound. The sounds were also subsequently ranked based on the following characteristics of an “ideal” therapeutic sound:

- Decline in tinnitus loudness. The best sound for this measure (ranked #1) would result in the greatest total decrease in perceived tinnitus loudness between threshold and MML; the worst sound (ranked #4) would result in the smallest total decrease.
- Increase in sound loudness. The best sound for this measure (ranked #1) would result in the smallest total increase in perceived sound loudness between threshold and MML; the worst sound (ranked #4) would result in the greatest total increase.
- Decline in tinnitus annoyance. The best sound for this measure (ranked #1) would result in the greatest total decrease in perceived tinnitus annoyance between threshold and MML; the worst sound (ranked #4) would result in the smallest total decrease.
- Increase in sound annoyance. The best sound for this measure (ranked #1) would result in the smallest total increase in perceived sound annoyance between threshold and MML; the worst sound (ranked #4) would result in the greatest total increase.

The MP3 volume was initially set for BBN and the nature sound to be one step (10%) below Equal Loudness Level, and if participants preferred it to be slightly higher or lower due to comfort reasons, the sounds were further adjusted accordingly. The final sound set was therefore at an audibility where sound interfered with tinnitus perception but that was also comfortable for the user.

9.4.3.3. Assessments

Initial Assessments

Following a comprehensive case history (Tinnitus Case History Questionnaire; TCHQ; (122) a hearing assessment was conducted in a sound treated room (ISO 8253–1:2010). Pure tone audiometry (0.25–16 kHz, (585)) was undertaken using a GSI-61 two-channel audiometer and TDH-50P headphones or E.A.RTONE 3A insert earphones and Sennheiser HDA-200 high-frequency headphones. Tympanometry was undertaken using a GSI Immittance audiometer to check middle-ear function.

Tinnitus testing was carried out using tinnitus testing software (The University of Auckland) using high frequency circumaural headphones (Sennheiser HDA-200). Tinnitus pitch match was assessed throughout the test frequency range of 0.25 – 16 kHz using a two-alternative forced-choice (2AFC) method. Each tone was presented at a sensation level of 15 dB SL. Pitch match was then compared to tones one octave above and below to rule out octave confusion. The measurement was repeated until two repeatable responses were obtained. Loudness level matching (LLM) was obtained using the pitch-matched stimulus sound at 30 dB above the threshold level and decreasing it slowly in 2 dB steps until the participant stated
it was same loudness as their tinnitus. This was repeated three times, and the average of the last two runs was taken. This was subtracted from the threshold level to obtain a level match in dB SL. Minimum masking level (in dB SL) was obtained using a NBN stimulus, raising it from the threshold level until the participant reported that the tinnitus was no longer audible. This procedure was repeated three times, and the average level was calculated. This was subtracted from the threshold level to give the MML match in dB SL.

The Multidimensional Personality Questionnaire (MPQ) (48) was also administered at the initial appointment to measure levels of individual personality traits.

Attention

The Comprehensive Attention Battery (CAB®) (629) was used to behaviourally measure individual attention and concentration ability. The CAB is a reliable computer supervised test battery and can be repeated before and after intervention administration to assess for any resulting change. The Discrimination Reaction Time Task (measuring focused attention) and Reaction Time Task (measuring alertness needed for general cognitive task performance) (630) were utilized in this trial from the CAB series of tests, as in previous studies these domains showed the greatest interaction with tinnitus (631). Focused attention requires attention to be directed towards one aspect of sensory information while excluding others, and is analogous to selective attention (632). Alertness consists of three components: 1) Expectancy, 2) Orientation to various stimuli & 3) Readiness to produce a motor output. Decreased Reaction Time Task or Discrimination Reaction Time Task scores over time can therefore indicate loss of concentration or increased cognitive load, or inability to focus attention selectively, which can result if tinnitus is increased in magnitude.

For the Reaction Time Task, a grey square was presented in the middle of an otherwise dark/black computer screen. The visual assessment required the participant to respond as soon as possible (touching the square) when it quickly changed to a green colour. The presentation lasted 200 ms and occurred after a time delay randomly varying from 1 to 4 seconds (1000 to 4000 ms).

For the Discrimination Reaction Time Task, the visual task involved watching a grey square presented in the centre of a dark/black computer screen. Random visual presentations of 3 different coloured squares then occurred in the centre of the computer screen: red, blue or green. Participants were required to touch the grey square as soon as possible, registering
their response, if the square changed to the target colour (red) while ignoring non-target colours (blue or green). The target presentations lasted 200 ms, interspersed with 1800 ms time delays. In the auditory task condition, participants were instructed to listen for the target colour word (green) and ignore verbalizations of non-target colour words (red or blue).

Random auditory presentations (spoken) then occurred of 3 different colour words: Red, blue or green. Participants responded by touching the grey square whenever they heard the target colour word (green) and ignored verbalizations of non-target colour words (red or blue).

Word presentation lasted approximately 300 ms. In the mixed visual and auditory condition, participants heard verbal instructions “The Target Is” followed by either: 1) The grey square changing in colour to indicate a visual target, or, 2) An auditory presentation (spoken) denoting an auditory colour word target. Whenever the target was seen or heard (depending on whether the target given was visual or auditory in nature), the participant was required to press the square as quickly as possible. While anticipating the indicated target, participants experienced randomized presentation of visual and auditory non-targets; spoken colour words or visually presented colour changes for the grey square. Targets were altered 7 times during the assessment. The tasks resulted in assessment of pure visual reaction time (50 stimuli), pure auditory reaction time (50 stimuli) and visual and auditory reaction time (100 stimuli).

**Questionnaires for Clinical Evaluation**

The Tinnitus Functional Index (TFI) (110) was the primary outcome measure, in addition, the following questionnaires were used: Tinnitus Loudness Rating (scale of 1-10), Tinnitus Annoyance Rating (scale of 1-10), Positive and Negative Affect Schedule (PANAS) (633), and the Depression, Anxiety and Stress Scale (DASS Scale) (634). The TFI (110) is a recently developed questionnaire and assesses both severity of tinnitus and its impact on life over 8 diverse subscales of intrusiveness, sense of control, cognitive, sleep, auditory, relaxation, quality of life, and emotional. TFI shows high responsiveness to treatment-related change and has been validated as an intake questionnaire with good test-retest reliability in the NZ population (635). Tinnitus loudness ratings were made on a 10-point rating scale where 1 corresponded to a very quiet and 10 with extremely loud. Annoyance ratings were made on a similar scale with 1 being very low in distress and/or annoyance and 10 being extremely high in distress and/or annoyance. PANAS measures the extent to which positive and negative emotional states are experienced by an individual over the period of the past week. The DASS scale measures levels of affective symptoms.
Qualitative Interviews

At each follow-up appointment and at the end of the trial all participants were interviewed, and the interviews were digitally recorded, transcribed and responses coded into themes. The interview schedule for each follow-up appointment was as follows:

1. How often did you use sounds stimuli?

2. In which particular environments did you find yourself using the sounds?

3. How is the quality of the intervention sound?

4. How you feel the sound is interacting with your tinnitus?

5. Has the quality (characteristics of your tinnitus such as the pitch, duration, fluctuation, etc.) of your tinnitus changed over the last month? If yes, how?

Additional questions asked during the final end-of-trial interview were:

6. Which of the two stimuli (BBN or nature) did you prefer the most? Why?

7. Will you be willing to wear this device as a form of tinnitus management for the next 6 months? Why or why not?

8. How can each of the sound stimuli be improved and why would this be an improvement?

9. Any other comments?

9.4.3.4. Trial Protocol

A randomized controlled, cross-over study design using mixed (qualitative and quantitative) methods was employed. Each sound therapy was administered for eight weeks each via a Philips ViBE SA4VBE08KF/97 4GB MP3 Player and Panasonic RP-HJE290GUK Premium Black Earphones with a Budloks Earphone Sports Grip earpiece attached for secure retention within the ear. There was a three week wash-out period in between the two conditions. Participants were instructed to listen to the sound therapy for a minimum of one hour per day.

Repeated outcome measures were obtained at three time points: baseline when the sound was first fitted, 4 weeks after administration and 8 weeks after administration for both Predictable
and Unpredictable sound therapies. The time-frame protocol for data collection and the outcome measures taken at each appointment are reported in Figure 36 and Table 9.

The order of sound presentation for participants (Order 1 = BBN then Nature OR Order 2 = Nature then BBN) was decided using an online, free True Random Number Generator (https://www.random.org/). There were no significant differences in personality trait scores between participants placed in Order 1 compared to Order 2. Throughout the trial the same researcher tested all participants. The only blinding applied was participants were not shown the results of their tinnitus outcome measures at the different time points until the end of the trial. Blinding to intervention type could not be provided due to the distinct perceptual sound characteristics of the two sound stimuli. No tinnitus counselling was provided; participants had their hearing tests and tinnitus results explained, and instructions were provided on use of the MP3 player and how to set volume relative to their tinnitus. The nature sound trialled was that chosen by the user.

**Figure 36.** Protocol for data collection. Multiple outcome measurements were taken at the following time points: 1st sound fitting (Baseline), and 4 weeks and 8 weeks after first fitting while the sound was being used. A washout period of 3 weeks followed in which no sound was administered. Multiple outcome measurements were then taken at the following time points: 2nd sound fitting (Baseline), and 4 weeks and 8 weeks after second fitting while the sound was being used.
9.4.4. Statistical analysis

A 2x3 repeated-measures Analysis of Variance (ANOVA) was used to examine changes in outcome measures between the two sound types (BBN, natures sounds) at the three time points (baseline, 4 weeks of intervention and 8 weeks of intervention). All assumptions were tested for all outcomes for each independent variable to see if they were met before running ANOVA. In cases where a significant main effect was observed, Bonferroni post-hoc tests were administered.

For outcome measures where there was no group effect for intervention observed at 8 weeks, further bivariate correlation and ANOVA analyses of changes in outcome measures (8 weeks-baseline) was conducted in order to explore whether age, gender and degree of hearing loss (categorized as slight, mild, moderate, moderately severe, severe or profound (636) based on average of 3000, 4000 and 6000 Hz hearing thresholds bilaterally) effects were present. These frequencies are used to calculate the average high-frequency threshold in audiometric testing.

In order to extract potential converging information of the different outcome measures and identify key factors influencing the effect of sound therapy administration on tinnitus over time, a Principal Component Analysis (PCA) was conducted. Changes in all outcome
measures (regardless of BBN or Nature sounds) between 8 weeks and baseline as well as baseline measures of personality were included. All components with Eigenvalue greater than 1 were extracted. Following inspection of data and the scree plot, a decision was made regarding the final number of components to be included in rotational analysis with Direct Oblimin rotation. Correlations about 0.5 were criterion used to define and load key variables to respective components and construct dimensions.

The framework method (586) was used to analyse the qualitative interviews, consisting of five steps: familiarization, identification of a thematic framework, indexing, charting, and mapping and interpretation. Familiarization involved careful listening to the digital recordings and transcribing, and re-reading the transcription. Common themes were identified in the transcripts, and in the charting phase, the data was rearranged according to theme. In the mapping and interpretative stages, the charted data was compared and contrasted to identify patterns within the data. Quotations from participants and their thematic analysis were included in the results following standard practice in qualitative methodology (637, 638).

9.5. Results

9.5.1. Loudness and Annoyance Functions for Sound Therapy Stimuli and Tinnitus

All the sounds resulted in decreased tinnitus loudness and annoyance, and increases in sound loudness and annoyance occurred as noise level was raised (Figures 37 and 38; Tables 10 and 11). When the sounds were ranked based on average rating changes with noise level increases, Rain was ranked #1 for tinnitus loudness decline, #4 for sound loudness growth, #1 for tinnitus annoyance decline and #2 for sound annoyance growth. Cicadas was ranked as #1 in tinnitus loudness decline, #4 in for sound loudness growth, #1 for tinnitus annoyance decline and #1 for sound annoyance growth. Surf was ranked #4 for tinnitus loudness decline, #1 for sound loudness growth, #4 for tinnitus annoyance decline and #2 for sound annoyance growth. BBN was ranked #1 for tinnitus loudness decline, #1 for sound loudness growth, #1 for tinnitus annoyance decline and #4 for sound annoyance growth.
At MML, sound ranking based on lowest tinnitus loudness rating was: BBN (best) >Cicadas/Rain>Surf (worst). Lowest tinnitus annoyance rating at MML was: Rain/Cicadas/BBN (best) >Surf (worst). For lowest sound loudness measure at MML, the ranking was: Rain/Cicadas/Surf (best) >BBN (worst). For lowest sound annoyance measure at MML, the ranking was: Rain (best) >Cicadas/Surf>BBN (worst). The Equal Loudness Level ranking was: Rain/BBN>Cicadas>Surf. The Equal Annoyance Level ranking was: Surf>Rain>Cicadas>BBN.

9.5.2. Selection of Nature Sound

Eleven out of the 18 participants (61%) preferred the Rain sound. Five participants selected the Surf sound (28%) while 2 selected Cicadas (11%). Rain had the highest valence rating (most pleasant) by participants, followed by the Surf and Cicadas respectively. BBN was the least pleasant of all the sounds (Figure 39). Key reasons for selecting Rain were that it was soothing and interacted more with tinnitus:

“The most pleasant, easier to listen to, happy to be inside when it is raining outside where its warm and dry”

“Selected rain in the end – tinnitus has various pitches so rain might be better for masking across frequencies & is pleasant”

Sixteen out of 18 participants (89%) had associated memories of the sound selected, such as:

“Rain means garden is being watered and I’m inside and especially if you are in bed and hear the rain on the roof, happy thoughts”

“Happy place, walks in the forest... Warm, summery sort of sound”

“All my life, really... Grew up in a place where it rains a lot, can be quite a pleasant sound, water sounds”

Table 10. Change in tinnitus and sound loudness and annoyance as point changes on rating scales (1-10) and Equal Loudness Level and Equal Annoyance Level (measured as % of total sound level). For example, the Surf sound had the most gradual perceived increase in sound loudness, and resulted in the smallest change in tinnitus loudness and tinnitus annoyance. The surf sound also had the lowest Equal Loudness Level (the sound becoming louder than tinnitus at a lower % of MML) but the highest
Equal Annoyance Level (the sound was closer to MML before it became more annoying than the tinnitus). The number in brackets represents ranking from 1 (best on measure for sound therapy) to 4 (worst on measure for sound therapy).

<table>
<thead>
<tr>
<th></th>
<th>Rain</th>
<th>Cicadas</th>
<th>Surf</th>
<th>BBN</th>
</tr>
</thead>
<tbody>
<tr>
<td>As point changes on rating scale (1-10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Tinnitus Loudness</td>
<td>5 (1=)</td>
<td>5 (1=)</td>
<td>4 (4)</td>
<td>5 (1=)</td>
</tr>
<tr>
<td>Decline</td>
<td>4 (1=)</td>
<td>4 (1=)</td>
<td>3 (4)</td>
<td>4 (1=)</td>
</tr>
<tr>
<td>Total Sound Loudness</td>
<td>8 (4=)</td>
<td>8 (4=)</td>
<td>5 (1)</td>
<td>6 (1)</td>
</tr>
<tr>
<td>Growth</td>
<td>2 (2=)</td>
<td>1 (1)</td>
<td>2 (2=)</td>
<td>5 (4)</td>
</tr>
<tr>
<td>As % of total sound level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Equal Loudness Level</td>
<td>35 (1=)</td>
<td>30 (2)</td>
<td>25 (4)</td>
<td>35 (1=)</td>
</tr>
<tr>
<td>Equal Annoyance Level</td>
<td>67 (2)</td>
<td>53 (3)</td>
<td>73 (1)</td>
<td>40 (4)</td>
</tr>
</tbody>
</table>
B.

**Cicadas on farm: Loudness Growth Curve**

- Equal Loudness Level
- Tinnitus and Noise Loudness
- Tinnitus Loudness
- Noise Loudness

![Cicadas on farm: Loudness Growth Curve](image)

C.

**Surf: Loudness Growth Curve**

- Equal Loudness Level
- Tinnitus and Noise Loudness
- Tinnitus Loudness
- Noise Loudness

![Surf: Loudness Growth Curve](image)
Figure 37. Loudness ratings growth curves for each therapy sound (Rain (A), Cicadas on Farm (B), Beach (C), BBN (D)) as a function of noise level (% between hearing threshold and minimum masking level for tinnitus). Loudness functions show decreases in tinnitus loudness (solid black line), increases in sound loudness (solid grey line), and increases in combined tinnitus and sound loudness as a function of sound level (dashed line). The Equal Loudness Level (square symbol) defines the sound level at which both tinnitus and sound were of equal perceived loudness (tinnitus and sound loudness rating = 5).
A.

Rain: Annoyance Growth Curve

- - - Equal Annoyance Level  Tinnitus Annoyance  Noise Annoyance

B.

Cicadas: Annoyance Growth Curve

- - - Equal Annoyance Level  Tinnitus Annoyance  Noise Annoyance

C.
Figure 38. Annoyance ratings growth curves of each therapy sound (Rain (A), Cicadas on Farm (B), Beach (C), BBN (D)) as a function of noise level (% between hearing threshold and minimum masking level for tinnitus). Annoyance functions show decreases in tinnitus annoyance (solid black line) and increases in sound annoyance (solid grey line) as a function of sound level. The equal annoyance point (square symbol) defines the sound level at which both tinnitus and sounds were of equal perceived annoyance (point of intersection between tinnitus annoyance and sound annoyance functions).
Table 11. Ratings on a scale of 1-10 of tinnitus and sound loudness and annoyance at the MML of tinnitus. For example, BBN at MML was rated as being louder and more annoying than other sounds; however, the administration of BBN at this level also resulted in one of the lowest tinnitus loudness and annoyance ratings.

<table>
<thead>
<tr>
<th>Rating at MML (on scale of 1-10)</th>
<th>Rain</th>
<th>Cicadas</th>
<th>Surf</th>
<th>BBN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tinnitus Loudness</td>
<td>2 (3=)</td>
<td>2 (3=)</td>
<td>3 (4)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Sound Loudness</td>
<td>8 (1=)</td>
<td>8 (1=)</td>
<td>8 (1=)</td>
<td>9 (4)</td>
</tr>
<tr>
<td>Tinnitus Annoyance</td>
<td>1 (1=)</td>
<td>1 (1=)</td>
<td>2 (4)</td>
<td>1 (1=)</td>
</tr>
<tr>
<td>Sound Annoyance</td>
<td>3 (1)</td>
<td>4 (2=)</td>
<td>4 (2=)</td>
<td>6 (4)</td>
</tr>
</tbody>
</table>

All participants except one (who expressed neutral feelings) reported the nature sound was pleasant, soothing, relaxing and elicited happy feelings. The ratings of sounds and personal preferences of individuals were in agreement. The sound rating feature that appeared most important for selection based on preferences was level of pleasantness (participants were more likely to select the sound which was perceived as being highly pleasant).

Figure 39. Average valence ratings of sound therapy stimuli by participants. Error bars represent +/- one standard error.
9.5.3. Intervention Outcomes: Tinnitus measures

There was a significant main effect of sound therapy time on TFI scores, with a 5.7 point decrease in TFI scores at 8 weeks compared to baseline (F(2,28)=4.144, p < 0.05) (Figure 40). There was a significant effect of sound types at 8 weeks (F(1,28)=6.875, p < 0.05), with BBN sound administration resulting in a mean 8.2 point decrease in scores, while nature sounds resulted in a 3.2 point decrease. The small change in TFI in response to the nature sounds at 4 weeks (4.2 point decrease) was not statistically significant. There was no significant difference in tinnitus measures between before the washout (8 week follow-up appointment for the first sound) and immediately after the washout (sound fitting appointment for the second sound). There was also no effect of order: the degree of change in tinnitus outcome measures was not significantly different between the first and second sound administered. Given the similarity in frequency composition of Rain to BBN (both are also fairly constant over time), outcome measures at 4 and 8 weeks for participants who selected Rain was compared to the other nature sounds (Surf and Cicadas). There were no statistically significant differences between the groups.

There was no difference in loudness or annoyance ratings following sound therapy at 4 weeks compared to baseline. There was no difference in loudness or annoyance ratings following sound therapy at 4 weeks compared to baseline. At 8 weeks the loudness ratings were 13% lower than at baseline irrespective of the BBN or nature sound condition (F(2,28)=1.551, p < 0.05) (Figure 41). At 8 weeks, annoyance ratings were 25% lower than at baseline irrespective of BBN or nature sound condition (F(2,28)=2.815, p < 0.05). There was no significant difference in tinnitus loudness ratings and annoyance ratings between BBN or nature sound conditions at either 4 weeks or 8 weeks.

There was a significant effect of sound types on loudness level matches at 8 weeks (F(1,28)=3.134, p < 0.05), with BBN sound administration resulting in a greater mean increase in loudness level match (2.6 dB increase in LLM) while nature sounds had slight increase (0.47 dB increase in LLM) (Figure 42). There was no significant difference between BBN or nature sound conditions at 4 weeks. Overall, there was no significant main effect of sound therapy on loudness level matches at either 4 weeks or 8 weeks. There was no significant change in minimum masking levels between 4 weeks and baseline. There was no
significant difference between minimum masking levels with sound types at either 4 or 8 weeks.

**Figure 40.** (A) Individual TFI scores of participants at baseline, at 4 weeks follow-up and at 8 weeks follow-up following administration of BBN and nature sound stimuli. Horizontal lines represent average TFI scores. (B) Average TFI scores of participants at baseline, at 4 weeks follow-up and at 8 weeks follow-up following administration of BBN (black) and nature (grey) sound stimuli. The significant difference is indicated by (*, p<0.05). Error bars represent +/- one standard error.
Figure 41. Tinnitus loudness ratings (on a scale of 1-10, where 1 corresponded with very quiet tinnitus and 10 with extremely loud tinnitus) and annoyance ratings (on a scale of 1-10, where 1 corresponded to low in distress and 10 with extremely high distress) of participants at baseline, at 4 weeks follow-up and at 8 weeks follow-up. Significant differences are indicated by (*, p<0.05). Horizontal lines represent average rating scores.

Figure 42. Average LLMs (in dB SL) at baseline, at 4 weeks follow-up and at 8 weeks follow-up following administration of BBN and nature sound stimuli. Horizontal lines represent average tinnitus
There was a significant main effect of sound therapy time on tinnitus positive emotionality scores (F(2,28)=2.210, p < 0.05) with lower levels reported 8 weeks compared to baseline (1.4 points) (Figure 43). There was no significant difference between sound types on positive emotionality scores at either 4 or 8 weeks. There was a very small but significant effect of sound therapy time on negative emotionality scores (F(2,28)=1.247, p < 0.05), with an increase in scores at 8 weeks compared to baseline (0.2 points). There was no change in negative emotionality scores between 4 weeks and baseline. There was no significant difference between sound types on negative emotionality scores at either 4 or 8 weeks.

There was a significant effect of sound therapy time on all outcomes measures of anxiety, depression and stress (Figure 44).

Reduced anxiety scores were observed between 4 weeks and baseline (0.3 points), and 8 weeks and baseline (1.1 points) (F(2,28)=3.721, p < 0.05); reduced depression scores were observed between 4 weeks and baseline (0.6 points), and 8 weeks and baseline (1.4 points) (F(2, 28)=2.44, p < 0.05); stress scores were increased between 4 weeks and baseline (2.3 points), and decreased between 8 weeks and baseline (1.1 points) (2,28)=3.01, p < 0.05).

There were no significant effects of sound therapy time or sound type on either attention reaction response times or attention discrimination response times. Although 8 weeks of BBN appeared to result in slower attention reaction response times, the differences were not statistically significant (Figures 45 and 46).
Figure 43. Positive Emotionality and Negative Emotionality scores at baseline, at 4 weeks follow-up and at 8 weeks follow-up. Horizontal lines represent average scores. Significant differences are indicated by (*, p<0.05).

Figure 44. Anxiety, depression and stress scores of participants at baseline, 4 weeks follow-up and 8 weeks follow-up. Horizontal lines represent average scores. Significant differences are indicated by (*, p<0.05).
Figure 45. Box plot showing minimum, lower quartile (25%), median, upper quartile (75%) and maximum CAB Reaction Time Task response times (ms) of participants at baseline and after 8 weeks administration of nature (white) and BBN (grey) sound stimuli.

Figure 46. Box plot showing minimum, lower quartile (25%), median, upper quartile (75%) and maximum CAB Discrimination Time Task response times (ms) of participants at baseline and after 8 weeks administration of nature (white) and BBN (grey) sound stimuli.
9.5.5. Principal Component Analysis

The Kaiser-Meyer-Olkin measure (KMO) verified the sampling adequacy for the analysis (KMO = 0.62). Bartlett’s test of sphericity indicated that inter-measure correlations were sufficiently large for PCA (p < .001). The majority (87.5%) of variation in outcome variables following sound therapy administration over time were accounted for by changes in tinnitus impact on life (27%), tinnitus perceptual characteristics (9%), stress reduction/relaxation (21%), changes in positive mood (16%) and changes in negative mood (14%). This was a satisfactory amount of variation. The individual correlations/strength of loadings of each intervention outcome measure on to each principle component is provided in Table 12.

Table 12. Principal Components Analysis (with Direct Oblimin Rotation) Loadings of Intervention Study Outcomes. Eigenvalue>1 criteria applied. Correlations above 0.5 and total variance explained by principal components are presented in bold.

<table>
<thead>
<tr>
<th></th>
<th>Tinnitus Impact on life</th>
<th>Tinnitus Perceptual characteristics</th>
<th>Stress Reduction/Relaxation</th>
<th>Positive Mood</th>
<th>Negative Mood</th>
</tr>
</thead>
<tbody>
<tr>
<td>TFI Total Score</td>
<td>-0.787</td>
<td>.608</td>
<td>.076</td>
<td>.027</td>
<td>0.003</td>
</tr>
<tr>
<td>Tinnitus Loudness Ratings</td>
<td>-0.493</td>
<td>.860</td>
<td>0.05</td>
<td>-.050</td>
<td>0.990</td>
</tr>
<tr>
<td>Tinnitus Annoyance Ratings</td>
<td>0.984</td>
<td>0.10</td>
<td>-.052</td>
<td>-.053</td>
<td>-.085</td>
</tr>
<tr>
<td>Tinnitus Loudness Level Match</td>
<td>0.984</td>
<td>0.10</td>
<td>-.052</td>
<td>-.053</td>
<td>-.085</td>
</tr>
<tr>
<td>Tinnitus Minimum Masking Level</td>
<td>0.134</td>
<td>.967</td>
<td>.047</td>
<td>-.031</td>
<td>-.115</td>
</tr>
<tr>
<td>Positive Emotionality</td>
<td>-0.032</td>
<td>.083</td>
<td>-.310</td>
<td>.898</td>
<td>.039</td>
</tr>
<tr>
<td>Negative Emotionality</td>
<td>.118</td>
<td>.112</td>
<td>-.032</td>
<td>-.318</td>
<td>.788</td>
</tr>
<tr>
<td>Depression</td>
<td>-0.050</td>
<td>.109</td>
<td>.601</td>
<td>-.730</td>
<td>-.017</td>
</tr>
<tr>
<td>Anxiety</td>
<td>-.171</td>
<td>.053</td>
<td>.887</td>
<td>-.102</td>
<td>.142</td>
</tr>
<tr>
<td>Stress</td>
<td>0.091</td>
<td>-.037</td>
<td>.856</td>
<td>-.270</td>
<td>.282</td>
</tr>
<tr>
<td>Attention Reaction Response Times</td>
<td>-.547</td>
<td>.061</td>
<td>.584</td>
<td>-.278</td>
<td>-.397</td>
</tr>
<tr>
<td>Attention Discriminatory Response Times</td>
<td>-.074</td>
<td>-.447</td>
<td>.258</td>
<td>.685</td>
<td>-.246</td>
</tr>
<tr>
<td>Personality: Stress Reaction</td>
<td>.073</td>
<td>-.027</td>
<td>-.730</td>
<td>-.041</td>
<td>.558</td>
</tr>
</tbody>
</table>

$h^2$
The effects of age, gender or hearing loss on outcome measure changes were investigated. Participants with mild hearing loss had a decrease in LLM (5.7 dB SL), while those with moderately severe hearing loss showed a slight increase in LLM (0.83 dB SL) between baseline and 8 weeks (F(3,15)=2.32, p < 0.05). During administration of BBN and natures sounds, significant differences by gender were present for negative emotionality (F(1,15)=6.393, p < 0.05); females displayed an increase in scores between baseline and 4 weeks (2.4 point increase), while males had a decrease in scores between baseline and 4 weeks (4.4 point decrease). Significant differences by gender were present for depression (F(1,15)=3.096, p < 0.05), anxiety (F(1,15)=5.532, p < 0.05) and stress (F(1,15)=6.37, p < 0.05). Females had a slight increase in depression scores (0.52 points) and anxiety scores (0.82 points) between baseline and 4 weeks; males had a decrease in depression scores (3.35 points) and anxiety scores (2.09 points) for the same time period. Females had an increase in stress scores (2.96 points) between baseline and 8 weeks; males had a decrease in stress scores (2.42 points) for the same time period.

### 9.5.6. Individual differences

For all outcome measures where there were no effects of sound types after 8 weeks of trial, individual results were explored in a descriptive manner for any patterns (Figure 47). Overall, there was a considerably large amount of individual variability present in responses to sound therapy.

A greater number of participants seemed to experience a decrease in tinnitus loudness ratings at 8 weeks compared to baseline (than an increase or no change); this was slightly more likely to occur during administration of nature sound than BBN. For those who experienced an increase in tinnitus loudness rating with the presence of sound, this was most likely to occur regardless of whether BBN or nature sound was administered. Likewise, more participants
seemed to experience a decrease in tinnitus annoyance ratings at 8 weeks compared to baseline (than an increase or no change); however, this was more likely to occur during administration of BBN sound. For those who experienced an increase in tinnitus loudness rating with the presence of sound, this was most likely to occur for a specific sound type (either BBN or nature sound, but not both).

More participants seemed to experience a decrease in MML and anxiety scores at 8 weeks compared to baseline; for both these outcome measures, a decrease was more likely to occur during administration of BBN than nature sound. For negative emotionality, positive emotionality, depression, stress, attention reaction and discrimination response time scores, individuals were roughly equally distributed by whether there was an increase, a decrease or no change between 8 weeks and baseline. One participant had a significant decrease in depression scores under the BBN condition; the decrease in depression scores seemed to be considerably less for nature sound administered to the same individual. Another participant had a considerable decrease in depression scores with nature sound; BBN however led to an increase in depression scores in the same person.

A.

![Chart showing change in tinnitus loudness rating at 8 weeks](chart.png)
B. Change in Annoyance Rating at 8 weeks

C. Change in MML at 8 weeks
D.

Change in Negative Emotionality at 8 weeks

Participant Number

E.

Change in Positive Emotionality at 8 weeks

Participant Number
F. Change in Anxiety at 8 weeks

G. Change in Depression at 8 weeks
H.

Change in Stress at 8 weeks

Participant Number

I.

Change in Attention Reaction Time at 8 weeks

Participant Number
9.5.7. Intervention Outcomes: Qualitative Reports

Following qualitative analysis using the framework method, certain key areas emerged with regards to the sound trial. Common threads identified during the qualitative interviews are outlined below, along with relevant excerpts.

Hours & Environments of use

Most participants used both sounds for the minimum amount required each day and reported usage ranged from 0.5-1.5 hours for BBN. The nature sounds were listened to for longer periods of time: 9 participants reported consistently using the nature sound for 2 hours or more. One participant used the sounds at work (7 hours/day). If participants were involved in engaging activities, they often let the sounds run on.

“Sometimes let it go on if reading, etc. at other times interrupted.”
“An hour a day... If sitting and in between patterns with knitting, keep looping”

The vast majority of participants used the sounds in more than one environment: 44% in quiet, usually in the evenings or in bed reading, 28% working on quiet tasks around the house, garden or in the car, and 28% at the office or doing computer work. A few participants reported experimenting with the sounds in some situations with extra sound such as TV, radio, while having conversations, in traffic noise. The use of sounds in the presence of noise did not make the tinnitus worse.

“Have tried when walking dogs but traffic noise is too loud”

“Sometimes wear it to café for tea, lunch as well, general group asked once explained normal voice – could hear them fine, so it’s been quite good.”

“Have worn it while watching TV, did not find any interference.”

**Early Termination of Trial**

For 17% of participants (3 participants), the trial had to be terminated early due to significant exacerbation of tinnitus. In two out of the three cases, termination occurred during administration of BBN sound. The reason for variation was a specific life event (death of brother-in-law, disruption to sleep activity) and an incident (workplace incident exposure to loud noise). The third case terminated during nature sound administration, as they had disruption to sleep activity and did not observe any benefit.

“The tinnitus became worse 4 weeks after use. During this time, I was exposed to a high pitched noise in the lab, from a chiller, where I work on a daily basis (about 1 hour per day), and some of the time I could not wear hearing protection as I was having site meetings. This instantly made the tinnitus worse. Even having to wear earmuffs in lab after as a result, it shuts out ambience noise and focuses on tinnitus, so I’m more aware of it.”

“Unfortunately, my tinnitus seems to have got worse lately, particularly at night. I have been waking up in the early hours and then having trouble getting back to sleep... The reason gave it away in the end, is because I started to wake up in the middle of night – tinnitus was there and trouble getting back to sleep again – never had that problem before so think it is because of the sound, but I am not sure whether it is the tinnitus that wakes me or because of the recent stress in my life. Anyhow I have decided to stop using the sound.”

“Woke up last night and it was horribly loud. It isn’t beneficial to continue.”

**Effectiveness of intervention Sounds at 4 weeks**
At 4 weeks 42% of participants reported experiencing a worsening of tinnitus with both sounds (Figure 48). Among those who reported no change in tinnitus (39%), a slightly higher proportion reported this during administration of BBN than nature sound. In contrast, slightly more participants (19%) obtained tinnitus relief with nature sound compared to BBN.

“More often than not it actually has reduced in level”

“White noise moved tinnitus back from when I started”

“It certainly does make a difference, I think the sound of tinnitus has changed, seems quieter – maybe because you are feeling more relaxed”

“I don’t have severe days as much - loudness might have levelled out”

“Not as harsh as it was, softened it”

Six participants who continued with the trial until the end still felt tinnitus was exacerbated with BBN sound and 9 participants with nature sound. For some participants the increase in tinnitus was not observed while the sound was playing, but immediately, or shortly, after the sound was stopped.

“Last month have started annoying me, more stress because can hear it more.”

Attention on the tinnitus on it increased, so increased sensitivity to the tinnitus – first week was really intense, starting to really annoy.”

“No change in tinnitus while sound is playing, after stopped listening tinnitus was louder. Earmuffs after lawn mowing have the same effect – perhaps due to blockage of the ear. For example, I slept with ear plugs and tinnitus was louder in the morning but goes away. Sleep patterns have been good.”

There was no noticeable change in tinnitus among 6 participants listening to BBN sound and 5 participants listening to nature sound.

“Tinnitus is more or less the same.”

“Do not think tinnitus has changed due to wearing the device.”

“Don’t think tinnitus greatly changes, can still hear tinnitus if you concentrate on it. Tinnitus – feels it’s created by stress – one day to another stress changes, so changes day to day.”
Effectiveness of intervention Sounds at 8 weeks

At 8 weeks 52% of participants did not perceive any change (Figure 49). A lack of perceived change was more prevalent following administration of the nature sound than the BBN. The group that had benefit (13% of participants) was almost three times more likely to benefit from BBN than nature sounds. However BBN was also reported more likely to make tinnitus become worse (34%).

“No change in tinnitus. Never notice tinnitus when sound is playing, in a way its disappointment because really wanted it to work.”

“Don’t think tinnitus has changed over the last month, probably more aware of it because of having the sound in there but don’t think it has increased or decreased in intensity.”

There were no statistically significant underlying differences in baseline outcome measures (e.g. baseline TFI score, LLM, etc.) or demographic factors (e.g. age, gender, etc.) between participant groups who reported benefit, no change or worse tinnitus at 8 weeks follow-up.
Figure 49. Perceived effectiveness of sound therapy (benefit, no change or worse) for BBN (black) and nature sounds (grey) at 8 weeks.

Preference of Intervention Sound at 8 weeks

Preference for one sound was asked, regardless of its interaction pattern with tinnitus. Of the 18 participants, only 3 (26%) did not have any preference. Thirty-two percent of participants preferred the BBN and a slightly higher 42% preferred the nature sound. Chi-squared tests showed that participants were not significantly more likely to choose any one of BBN, nature sound or no preference as a response than the other.

Nature sounds were relaxing and had a distracting element that had a psychological benefit.

“Just more relaxing, other sound wasn’t necessarily as chilled. The Surf was more relaxing, natural environment. Don’t know if there was a huge improvement in tinnitus... Took you away from it [tinnitus] for a bit which I guess is the useful bit, distracts you from it for awhile.”

“I can let it go for 6-7 hours and can also have conversations with it, it was a refuge.”

“Found other sound [nature sound] was more restful to listen to over time, ups and down, overall sound was easier to get lost in it. Not sure if there was a huge difference between the two in terms of interacting with tinnitus.”

BBN sound was described as interacting better with the tinnitus, and led to a noticeable difference in tinnitus. Among those who preferred BBN, the nature sound was commonly described as the more pleasant sound, but BBN was more efficient for treatment. In contrast, others did not like the distracting effect of nature sound (BBN was more uniform) and found attention was directed towards the tinnitus instead.
“Think for the first sound started to notice a difference, this sound has had more of a beneficial effect because more aware of situations where I say tinnitus is different.”

“Prefer the white noise better, although like the rain, might be because sound is “boring” where the nature is interesting, so attend to aspects of sound.”

“Certainly white noise – for nature sounds there were other sounds in the background which shouldn’t have been there.”

“Rain was better personally, find it more pleasant to listen to and would like to use it more. Both did interact with noise in my head, white noise masks tinnitus better because of constant sound but both seem usable to me.”

“Sound [BBN] is wonderful. The last one had the rain which was lovely, wasn’t sure I would like white noise but did... I actually had it on and if I was doing something I wouldn’t take notice of the time and would have it on for more than hour... What it did compared to the rain was that I wasn’t dwelling on it, it wasn’t distracting... White noise is great there because it is constant... White noise better at blending with the tinnitus.”

“This sound [BBN] has been more in the background: the crickets intensified my awareness of the other sound. This has been a more level response [BBN] even after I have taken it off. Stress in work life is keeping me awake and once awake the tinnitus makes it difficult to fall asleep at the moment. When I wasn’t under stress the tinnitus was manageable. That sound [nature sound] was probably more relaxing and nice, has a visual association of a forest. Whereas plain noise [BBN] is just a sound and doesn’t have any such associations. But easier to have white noise and hear people, with cicadas had to keep it off to hear people at work.”

Participants also mentioned that they initially conceptualized BBN to be less pleasant to listen to, but discovered that it was more tolerable than they had imagined.

“When you think of white noise think it is something you don’t want to listen to but was quite pleasant”

“When first heard white noise thought it would be unpleasant and off-putting, but not like that at all.”

There were no significant differences in hearing observable by sound preference; those with poorer hearing on average were less likely to have a preference although this was not statistically significant (Figure 50).
Figure 50. Average audiometric thresholds (dB HL) of participants for three participant groups: those who preferred the BBN sound at 8 weeks, those who preferred the nature sound at 8 weeks and those who did not have any preference.

Long-term use of sound device for tinnitus management

Nine participants were interested in continuing using the device for long-term tinnitus management and believed their tinnitus would change as a result. There was roughly equal split as to whether participants wanted to listen to BBN or nature sound over time. Two participants were interested in continuing sound therapy but did not believe their tinnitus would change.

“There is no objection to listen to it in the long term, depends on whether there is any benefit – so far can’t say there is any change in my tinnitus. However I didn’t find it a burden to use it and am happy to continue.”

Eight participants were not interested in continuing, predominantly because there was either 1) no benefit, 2) tinnitus became louder in volume as a result of sound therapy and/or 3) sounds made them more aware of their tinnitus as discussed previously.

Quality of Intervention Sounds

There were no concerns regarding the quality of both sounds from the majority of participants; however one felt their volume control increased dramatically from one step to another for the BBN.
“White noise – going from 4 to 5 in volume was a big jump, needed more of a smoother jump – the volume could have been recorded at a lower level to give a bigger range of adjustment.”

“Both sound quality were really good, don’t know how you would change the quality. Neither were intrusive or unpleasant”

“Not too bad if I don’t do it for too long.”

9.5.8. Relationship between Intervention Outcomes and Qualitative Reports

No trends were observable when grouping participant’s tinnitus quantitative intervention outcome measures (loudness rating, annoyance rating and LLM of tinnitus) by whether participants reported benefit or not from sound. There were also no observable trends when grouping by participant preference for an intervention sound.

9.6. Discussion

The administration of sound therapy led to reduction in tinnitus over 8 weeks. This effect was largely due to BBN sound therapy which resulted in a 8.2 point reduction of TFI scores (110); this was significantly different to the 3.2 point reduction following 8 weeks of Nature sound administration. The TFI reflects impact of tinnitus on quality of life (110). Both the TFI changes were not large enough to meet one suggested clinical criterion for meaningful reduction in TFI outcome scores (a 13-point reduction (627)) but BBN did if a different criteria of 7-8 point change (639) is applied. For most participants sound resulted in small but significant changes in secondary outcome measures of tinnitus (reduced loudness rating scale and reduced annoyance rating scale) and psychologically related measures (increased positive emotionality, reduced anxiety, reduced depression and reduced stress) Unlike response to rating scales, the loudness level matches increased for BBN, while there was minimal increase for loudness level matches for Nature sounds between baseline and 8 weeks follow-up. There was no significant change in MML matches following sound therapy administration. For BBN, while there was a slight decrease in loudness level matches for nature sound between baseline and 8 weeks follow-up. The results showed large individual preferences.
In this study participants played the sounds for 1-1.5 hours/day, which is less than many tinnitus treatment paradigms suggest (e.g. Neuromonics Tinnitus Treatment and Tinnitus Retraining Therapy recommend 6-8 hours use) (216, 217). The time frame (8 weeks) of administration was also less than the 6 months or greater suggested by these treatments. The degree of change observed with sound may be different if used for longer periods of time per day or administered over a longer time frame (e.g. individual responses might converge or diverge over a greater amount of time).

**Individual Differences (Age, Gender, Hearing Loss)**

There were some interesting differences observed in gender and hearing loss with regards to some of the changes in outcome measures (640). For the psychological outcomes of negative emotionality, depression, anxiety and stress, females had an initial worsening of symptoms between baseline and 4 weeks, while males had a decrease. LLMs significantly decreased over 8 weeks among individuals with mild hearing loss (by 6 points) while those with moderately severe hearing loss actually had an increase in LLM (by slightly less than 1 point). The introduction of sound therapy was most beneficial in cases of mild deafferentation and/or auditory pathway damage. This may be interpreted in two ways: the tinnitus characteristics of those with lower levels of deafferentation may be more driven by attentional and psychological variables, such that new sound provides attention diversion and relief translating into lower tinnitus loudness measurements, or in instances of severe damage/deafferentation to the hearing system, sound therapy is not able to reach the appropriate cortical regions to elicit any changes, even when set a comfortable and audible listening level (200). This has implications clinically when setting levels for sound therapy, especially when user-set. The counter to increasing levels to create greater tinnitus interaction is that if the level is set too high, there is a risk of triggering negative emotion and discomfort to the sound itself (6, 21); thereby also preventing any AL shifts (5).

**Individual Effects (Personality Traits)**

The four personality traits examined in this study have been associated with tinnitus perception and distress. Tinnitus sufferers displaying higher levels of stress reaction, lower social closeness, lower self-control and higher alienation than individuals with hearing loss (but not tinnitus) (10, 93, 167, 367, 374, 377, 433). In this study, personality traits of self-
control and social closeness were significantly negatively correlated, and social closeness and alienation were positively correlated. This is similar to previous findings applying the MPQ to tinnitus groups (641). Females in this study had greater levels of social closeness than males. Males in this study had higher alienation than females. Welch & Dawes (167) observed an elevation in alienation scores among men in their general population sample of 32-year-olds. Males also displayed higher emotional suppression scores than females in the study by Durai & Searchfield (623). Thus, underlying personality differences appear to exist between males and females who experience tinnitus.

Participants with moderate hearing loss also had significantly higher self-control scores than those with severe hearing loss. Both genetic and environmental factors interact to create an individual’s personality (46, 52). Some of the personality traits identified in this study, such as stress reaction and social closeness, are difficult to change (167). If any change is possible, it will be gradual and dependent on the age of the individual – absolute level changes have been reported to be more pronounced during adolescence and the elderly years of life, due to biological maturation, social expectations and conditioning processes (47, 50, 372, 642).

Personality differences can add to the heterogeneity presented in tinnitus, although this has been given little attention. It may be valuable to attempt to understand this contributory factor further by incorporating personality into assessment and for sub grouping to see how it shapes tinnitus perception, distress and emotional response.

**Attention effects**

Attention (focused attention and general alertness) (630) was the only measurement dimension that did not change over the 8 weeks. However, there were significant correlations present between changes in reaction time task attention scores and changes in MML and stress scores at 8 weeks. At 8 weeks, changes in discrimination time task attention scores significantly correlated with changes in TFI, depression and anxiety scores. This suggests a complex interaction between attention, cognitive and psychological affect, tinnitus perceptual characteristics and tinnitus impact on life, as suggested in the ecological model of tinnitus (6).

**Interpretation under the Adaptation Level Theory**

Under the ALT model, the ‘presence of sound effect’ (decrease in tinnitus outcomes after administration of either sound therapy stimuli) suggests a shifting of internal AL steadily
away from the tinnitus and towards background noise stimulus (Figure 51). This may occur due to component weighting shifts and attention diversion. Increased positive psychological benefits may also create a facilitating residual effect, which also shifts AL. It is possible that characteristics of specific sound stimuli may work by placing greater emphasis on altering one pathway than another (e.g. BBN has been reported to aid in attention diversion; nature sounds were reported as eliciting high valence emotions). Durai et al. (10) explored the possibility that tinnitus distress and loudness may be underlined by different perceptual and decision making processes that can be represented by two distinct adaptation levels. An AL can exist for any sensory modality, but also within each modality (43, 315, 321, 322). The AL for distress might be more prone to contextual and indirect psychological influences, given the complexity of non-auditory region involvement such as the emotional, arousal, attention and memory networks (2, 78, 128, 204). De Ridder et al. (4) have outlined a ‘tinnitus core’ sub-network within the brain. It has been suggested that the minimal set of brain areas that needs to be simultaneously active in order for tinnitus to be consciously perceived. Affective components of tinnitus are represented by additional and overlapping networks. There is a possibility that tinnitus signal AL weighting decreases via the direct pathway towards external sound (involvement of core networks) while the affective component decreases occur via a residual pathway.

A concern in qualitative reports by participants was that sounds were effective when turned on, but not when turned off. In some cases, the tinnitus was exacerbated immediately after turning sound off, e.g. “When I use the sound the relief is instant, then I turn it off and the tinnitus is really loud”, “I think it is useful while the device is on, sometimes find it worsens (or I seem to be more aware) of the tinnitus immediately after stopping the device”. The term residual excitation has been applied to describe the transient increase in tinnitus severity following external sound presentation observed in a subset of tinnitus patients (643). Explained under the ALT, this is possibly due to the comparison of tinnitus with tinnitus in
Figure 51. Conceptualization of current study findings under an adaptation level theory (ALT) framework for tinnitus perception (5). Tinnitus is envisaged as a sensory stimulus with an existing internal adaptation level (AL) which acts as a reference point for all tinnitus-related judgments and is able to be manipulated by context and time. A high tinnitus AL results in tinnitus that is judged by the sufferer as being of high magnitude and/or eliciting high distress. Three key components set the final AL: 1) the focal component/stimuli being attended to (tinnitus), 2) background stimuli, as well as 3) residuals (various psychological and cognitive individual influences, including emotion, personality, past experiences, arousal and level of prediction elicited by sound stimuli). The ‘presence of sound effect’ (red arrows) illustrates steady shifts in AL away from the tinnitus and towards sound therapy stimuli, which can occur by directly increasing the weighting placed on external sound, via attention and auditory streaming shifts. A valence of sound effect increases weighting placed on external sound via the residual pathway. The latter occurs as external sounds provide psychological relief from tinnitus and can counteract tinnitus-related negative emotions, anxiety, stress and depression, thereby creating a facilitating residual effect which reduces tinnitus severity. The ‘predictability difference effect’ (blue arrow) illustrates a potential difference between BBN and nature sounds in terms of the amount of prediction errors elicited; this may also influence the degree of adaptation each sound undergoes over time. Shifts in AL away from tinnitus towards external sound would discontinue upon adaptation of the auditory system to the external sound itself. Auditory system adaptation to BBN and natural sound therapy may occur at different rates. Adaptation to BBN occurs sometime between 4 and 8 weeks after the first introduction of the sound, leading to the need to increase the sound level required to match tinnitus in Loudness Level Matching. There may be small but immediate valence effects, but nature sounds due to their intermittent nature may take longer to reach peak adaptation, such that at 8 weeks no change in Loudness Level Matching may be observed.
noise, rather than prior to the noise. The adaptation level is only temporarily maintained at a higher level before adapting to the silence. Use of sounds that gradual fade in volume when “turning off” may reduce attention towards tinnitus, preventing or delaying tinnitus from coming back at full intensity.

ALT stresses the active interaction between an individual experiencing tinnitus, cognition and their environment (both the immediate surroundings and broader factors, including their culture, beliefs, work and social environment). The influence of the environment and health factors was evident in qualitative reports by participants, e.g. “Still feeling sick from flu, not feeling well at all, so not sure how accurate tinnitus perception might be”, “Stressed at work, because in my view I feel tinnitus is stress or noise related, so hear it more”. In the outer environment, the physical location as well as time of day can alter the magnitude of tinnitus as well. These changes occur via influencing attention, cognitive reserve, levels of arousal/stress, health status and emotional status and are dependent on the individual themselves (125, 126, 136). The environment is more dynamic than broader, slow-changing social factors such as an individual’s cultural norms, beliefs, religion, relationship and moral support (139,120) and interactions with health professionals and their tinnitus management strategies (120). Overall the success of sound appears to be partially related to individual influences, which interact to determine final tinnitus magnitude and its impact. It is not yet possible clinically to prescribe sounds that are tailored to an individual’s tinnitus with confidence that they are the best sounds. However the use of rating functions described in this study, when applied, may enable for selection of sound therapy for individuals appropriate to their needs at that time.

Factors Influencing Sound Therapy Effect on Tinnitus

Two components relating to sound therapy effects on tinnitus were interpreted, influencing impact of life such as presence, distress and reactions to tinnitus (encompassing TFI scores, annoyance ratings and LLMs) in addition to altering perceptual tinnitus characteristics such as subjective loudness and maskability (TFI scores, loudness ratings and MML). However, we also cannot rule out placebo effects on either the qualitative or quantitative results, in scenarios where placebo effects are relevant, choice over treatment can increase these effects (644) which may account for qualitative preferences for the nature sounds, but does not
account for the greater effects on the TFI with the BBN sound. TFI scores were the only variable which loaded onto both components of impact of life and perceptual characteristics. This is in line with one of the aims of the TFI, which is to comprehensively cover the broad range of symptoms associated with tinnitus severity (110).

Based on the pattern of results it was also reasoned that three residuals of sound therapy effects on tinnitus were stress reduction/relaxation, and positive mood and negative mood. Under broad classification, the components map well onto the ALT model explanation of tinnitus-related and residual psychology-related effects of sound therapy discussed. The discrepancy in mood change (both positive and negative) in relation to sound therapy administration is interesting. Negative Emotionality and the personality trait of Social Closeness loaded strongly positively on the negative mood dimension, while Alienation as a personality trait loaded strongly negatively. In contrast, strong negative loadings of Stress Reaction on Stress reduction/relaxation and Self Control moderately positively loaded on positive mood. One possible interpretation is that stress and self control are indices for discerning subgroups of individuals with exacerbated tinnitus following sound therapy. The sequence of events resulting in increased tinnitus may follow the indirect residual pathway (driven by an increase in negative affect) and the presence of certain underlying personality trait levels (e.g. social closeness, stress reaction) may determine the extent to which this pathway occurs and the magnitude of shifts in weighting towards tinnitus. However, this is only speculation and further research is needed in this regard.

Attention reaction response times loaded moderately negatively on tinnitus impact of life and moderately positively on stress reduction/relaxation. Attention discriminatory response times loaded moderately positively on positive mood. One possible explanation for this observation is that decreased tinnitus impact and increased psychological well-being in general may be related to increased attentional response times. Various studies suggest that reaction time is shorter under conditions of physiological stress (645, 646).

**Sound adaptation as a confound**

The loudness level match is commonly used to psychoacoustically measure changes in tinnitus; however its interpretation in cases where external sound is administered for long periods of time can be difficult. Hoare et al. (647) observed the presence of a significant procedural learning effect for tinnitus loudness matching over time, and suggest that the first
assessment should be used to overcome learning effects, and the second used for measurements. Discrepancies between subjective loudness rating scores and loudness level match measures have been observed in the past, termed the tinnitus loudness paradox (5, 37, 114). Interpreted under ALT, the loudness paradox arises because subjective loudness judgments estimate the current tinnitus AL: it is made in a sound proof booth with no contextual noise stimuli (37, 114). In contrast, the objective match is made when an external test stimulus is introduced and the individual has to match it with the existing tinnitus AL. If the AL is initially set high, the matching sound level does not have to be increased as much before it is perceived as being of equal loudness as the tinnitus. However, if the matching sound undergoes adaptation to sound over time it would appear quieter, and would therefore have to be raised in order to match the intensity of tinnitus loudness (which undergoes slower adaptation) (5, 10). The auditory system may adjust to sound therapy stimuli over time; this would eventually stop further AL shifts and/or result in shifts back towards tinnitus.

It is highly likely that adaptation to the intervention sound may confound the interpretation of loudness level matches in this study. Underlying neural changes can occur through gain control, or adjustment of input-output sound functions of auditory neurons (135, 320). Studies have observed stimulus-specific adaptation effects at all levels of the auditory system from early auditory encoding (320) to the auditory cortex (135, 349). Adaptation of the auditory system to BBN and nature sounds may occur at different rates. Because BBN is a predictable sound, it is adapted to at a faster rate, and also leads to an increase when an external sound is used to match tinnitus in loudness level matching. Unpredictable natural sounds are adapted to more slowly; therefore no change in loudness level match is obtained.

Another related effect is that it is possible for intermittent tinnitus masking (either predictable or unpredictable) to facilitate an auditory continuity illusion (485) whereby the brain ‘fills in the gap’ where masking sound is applied and tinnitus appears as a continuous percept. This learning effect involves several networks in the brain that overlap with that of tinnitus, including the limbic structures, basal ganglia and prefrontal cortex (587). Davis et al. (588) observed more consistent benefit over 12 months if Neuromonics Tinnitus Treatment involved masking of tinnitus for the first two months followed by intermittent perception of tinnitus compared to where there is intermittent perception of tinnitus throughout treatment. It may be useful to run future trials in which sounds are changed often to maintain novelty and to prevent sound adaptation, continuity illusion, and facilitate AL shifts towards external sound.
Modelling of Sounds Under ALT

Sound levels for this study were initially set one step (10%) below Equal Loudness Level and if participants preferred it to be slightly higher or lower due to comfort reasons, the sounds were further adjusted in order to stop evoking negative response. The final sound setting was therefore at a level where sound interfered with tinnitus perception but which is also comfortable for the user. There is limited and conflicting evidence regarding the benefit of one intensity of sound over another for sound therapy (5, 23, 648); it is still not possible to compute the optimal sound level or parameters of sound stimuli for any given individual (20).

Based on environmental sound selection task and ratings provided by participants in this study, Rain was selected by most participants and had the highest valence rating. Rain also showed the lowest growth in perceived sound annoyance with increases in noise level, as measured by sound annoyance ratings at MML. Although BBN lead to a greater decrease in tinnitus TFI (and also the greatest decline in tinnitus loudness and annoyance over noise levels from threshold to MML), this sound had the lowest valence rating and displayed the greatest perceived sound annoyance growth with increases in noise level.

Interestingly, BBN and Rain both had Equal Loudness Levels; this level was higher than for the two other sounds. A higher Equal Loudness Level indicates that a greater amount of sound is needed to be applied before it is perceived as being equally loud as the tinnitus. However, the Equal Annoyance Level for Rain higher than that for BBN. Therefore, both sounds had equal loudness growth but Rain was more tolerable over a larger range of sound level than BBN, at least in the short-term. The study results suggest that computing an ideal level of sound based on interaction with tinnitus alone does no cater for individual preference and emotional affect (important factors determining whether participants will use the sound or obtain relief from it). A better sound level computation will involve taking into account valence ratings and perceived tinnitus and sound loudness and annoyance growth functions.

Using the ALT framework, the effectiveness of a sound therapy stimuli in shifting AL between tinnitus (focal) and external sounds (background) can be modeled using loudness and annoyance functions (as % noise levels from hearing threshold to tinnitus masking level).

The mathematical formula for the ALT is:

\[ A = X^p B^q R^r \]
The weighting coefficients \( p, q \) and \( r \) establish the relative contribution of each component towards the final adaptation level \((p+ q+ r =1)\). Under the ALT model, the Equal Loudness Level (both tinnitus and noise are of equal perceived loudness) represent components \( X \) and \( B \) respectively and are equivalent by definition. The Equal Loudness Level can therefore symbolize AL tinnitus loudness. The Equal Annoyance Level (both tinnitus and noise are of equal perceived annoyance) can be a measure of AL tinnitus distress.

As used in this study, setting levels based on both characteristics of Equal Loudness and Equal Annoyance Levels may be useful; however, this warrants further research. Loudness and annoyance function of the sound stimulus itself should increase very gradually in response to increases in level. This will enable AL weighting to shift effectively from tinnitus towards the background stimulus, as well as allow greater “room” for adjustment for comfort, user preference, etc. A steep increase in sound stimulus can elicit distress, which may activate the limbic and autonomic systems and increase tinnitus perception instead (196). Moreover, in order to be effective, Searchfield et al. (5) have suggested two criterion for therapeutic sounds: 1) Sounds should be at low level below the tinnitus, so as to displace adaptation to tinnitus in the direction of the therapeutic sound, and 2) Sounds should be paid attention to. Therefore it is crucial that the level of therapeutic sound stimulus does not exceed the perceived loudness of tinnitus during administration. On the other hand, if stimuli are presented at a level considerably lower than Equal Loudness Level, they may have insufficient interaction with tinnitus to induce any shift in its AL.

The Equal Annoyance Level and Equal Loudness Level can theoretically serve as good indicators of tinnitus loudness AL and distress AL at a given point in time. However the accuracy of these indicators to track changes in tinnitus clinically over time might be confounded by the fact that therapeutic sound can undergo sound adaptation as well (21). To obtain optimal sound levels, other residual variables should also be computed into this formula. Further research such as using computational models with several data (102, 134, 649) can enable for ideal sound therapy levels to be identified as well as for computing "automated" changes in level accordingly based on any changes in residuals or sound adaptation in the future.

It is useful clinically to present a variety of options to individuals for sound therapy, rather than a "one sound fit all approach" as although both BBN (same sound administered to all) and environmental (participants selected one sound from three) resulted in small but
significant tinnitus and tinnitus-related outcome improvements, in the interviews self selected sound was more relaxing and pleasant to listen to; general wellbeing is increased in line with the holistic approach taken by ALT.

Clinical implications and sub grouping of Tinnitus Characteristics

Sixteen percent of the participants experienced an exacerbation of tinnitus sufficient enough to terminate the trial early; however, this was mainly due to external situational factors or incidents. It was not possible to identify any characteristics (e.g. personality trait, age, gender, duration of tinnitus, other tinnitus variables) which isolated these individuals from others in the study. At 4 weeks after administration, there were different subgroups among participants in terms of how they self-reported response to sound therapy: 42% had worsening of tinnitus, 39% no change and 19% obtained relief. Moreover, at 8 weeks after administration, there was variation in responses: 52% had worsening, 34% had no change and 13% had relief from sounds. The number of participants reporting benefit was lower than anticipated based on hearing aid (28, 32, 650) and tinnitus aid (197, 622) studies. This may, at least in part, be due to mode of sound delivery. MP3 players and earbuds were used as a lower cost intervention than tinnitus aids. Improvements in implementation of MP3 players from a previous study were made based on participant reports (626); an easier user interface was implemented by switching from Apple iPod shuffles to the Philips ViBE MP3 Player (with more accessible manual controls) and use of retaining hooks with the earbuds. However even these improvements resulted in less use than hearing aids. Patient reports suggest the MP3 players were used 1-1.5 hours per day, significantly less than that usually recommended for sound therapy using ear-level devices (6-8 hours per day) (23, 209). The sounds also did not compensate for hearing loss. Threshold adjusted noise (233) is implemented in several tinnitus aids (e.g. Siemens, Phonak, Oticon). The flat frequency response we used may have led to less interaction with tinnitus in the region of hearing loss, but would be similar for both the intervention sounds. Tinnitus aids can use sound in a number of ways through inbuilt sounds or by streaming sounds (651). A future trial should build on the findings in sound selection described here using tinnitus aids streaming sounds that are downloaded to tablet computers or smartphones, e.g. from hearing aid manufacturers Apps (e.g. Tinnitus Balance App, https://www.phonak.com/us/en/support/apps.html) or independent online sources (e.g. TinnitusTunes, http://www.tinnitustunes.com).
Self-reported preference of sounds varied considerably. Nature sounds (preferred by 42%) were reported as being relaxing and/or provided distraction from the tinnitus. BBN (32%) interacted better with the tinnitus, however, and was reported more effective as a treatment for masking tinnitus. The final preference stemmed from those aspects of sound deemed more important by the individual. In approximately a quarter of the cases (26%), there was no preference for either of the sound: quiet was preferred. Interestingly, there was no correlation between the reported effects of sound or preference of sound and the intervention outcomes in this clinical trial.

These findings highlight that qualitative and quantitative measures do not always clinically equate. Melin et al. (652) observed similar discrepancies in their study in which hearing aids were fit to individuals with tinnitus for 6 weeks. In the interview, participants who used their hearing aids for more than 2 hours daily reported benefit from tinnitus but the rating scale data did not support this (no change in ratings pre- and post-fitting). The results were explained by the authors in terms of demand characteristics: when asked during interviews, subjects may tend exaggerate (or underestimate) the ability of the intervention to change tinnitus, while the scaling may not be as sensitive to these effects. The extent of this reporting bias might differ between numerical rating scales and qualitative interviews. The inclusion of systematic qualitative methods in sound therapy treatment paradigms may be more advantageous than quantitative measures in identifying shifts in environmental factors or significant change in factors outside of the individual which can influence tinnitus (653), such as individual health or stress determinants (e.g. changes in tinnitus characteristics present as a result of illness, as reported in this trial) or to identify concerns which arise (e.g. situational factors which may result in discontinuation of sound, as reported in this trial).

Subgroups have been identified among tinnitus sufferers, which vary based on pathophysiology, perceptual features, co-morbid conditions and how they respond to specific treatments (11, 98, 189, 482). The results support the existence of different classes of tinnitus, and the ALT may eventually be most supported as a fitting framework for only a particular tinnitus subgroup. Both auditory and non-auditory residual factors may shift the AL more readily among such individuals. Moreover, age, gender, hearing loss, personality traits, and duration of sound therapy may all (hypothetically) be factors which can help delineate subgroups.
In this trial tinnitus counselling was deliberately not provided. Current tinnitus treatment paradigms such as Tinnitus Activities Treatment (654) and Tinnitus Retraining Therapy (156, 185, 209) use sound therapy alongside counselling of some form. Some trials of these therapies have been criticized (30, 31) as the benefits of sound therapy, over and above counselling, have not been determined. The results reported here are independent of counselling but it is strongly advocated that the use of sound clinically should be in addition to (not instead of) counselling. Sound therapy involves more than passive exposure to sound (95, 216), and participants need to be informed of this, and counselled also about how to use the sound. For some of the participants sound therapy ended up diverting attention towards the tinnitus instead. Individually tailoring sound therapy and counselling to target different components of the ALT would be expected to demonstrate an additive effect in shifting AL weighting away from tinnitus if administered together, than if each was administered in isolation. Attention training (239, 333, 631) might enhance adaptation to tinnitus through the presence of sound effect, while psychoeducation (or mindfulness or Cognitive Behavioural Therapy) (178, 179, 234) might increase tinnitus adaptation through the valence sound effect.

9.7. Conclusions

Overall, the presence of sound had a positive effect on the TFI; after 8 weeks of administration, sound therapy with BBN resulted in a greater reduction of TFI than nature sound. The positive effect of sound on tinnitus was supported by secondary tinnitus and psychological-related outcome measures, but not interviews. BBN and nature sounds did not differ significantly on secondary outcome measures of tinnitus, emotion, attention and psychological state after 8 weeks of administration. Interpreted under an ALT framework, internal AL weighting shifts away from the tinnitus signal and towards the sound therapy stimuli may occur, via a direct pathway towards external sound (involvement of core networks) while the affective component of tinnitus decreases via the residual pathway. The auditory system may adjust to sound therapy stimuli over time; this may eventually stop further AL shifts and result in shifts back towards tinnitus. It such cases predictable BBN might undergo loudness adaptation at a faster rate than unpredictable nature sounds.

This study provides further evidence for the heterogeneous nature of tinnitus. ALT appears to provide a framework for sound selection that could be applied to improve future sound-therapies. In this study, the selection of sound therapy stimuli by individuals was found to
be, at least in part, governed by certain characteristics of the stimuli itself. Within a clinical setting, it is important to understand individual variation and that each person presents with different needs. Individual preferences were shown within this study that might be applied to improve outcomes if known apriori. It may be beneficial to have a wide range of sounds available in the clinic. The results of the Principal Component Analysis and ALT model interpretation are both compatible with an ecological framework of tinnitus, a multitude of factors (e.g. attention and personality, characteristics of and preference for sound stimuli) appeared to determine the magnitude and experience of tinnitus at any one time. Regular qualitative assessments will allow for a more comprehensive picture to be obtained regarding various factors influencing sound success. Selecting sounds based on the ALT model would involve weighing treatment sound stimuli and sound levels based on sound valence ratings, tinnitus and sound loudness and annoyance (dependent on the individual’s profile at a particular point in time) as well as alternating presentation of sounds that evoke positive feelings (through the valence sound effect) and sounds with high interaction with tinnitus (for a presence of sound effect) over time, dependent on the individual’s profile at a particular point in time. Trials of sound therapy selection based on Adaptation Level Therapy are needed.
Chapter 10. Discussion
The aim of this thesis was to use a novel Adaptation Level Theory (ALT) model of tinnitus to empirically explore tinnitus perception (5), which states that any magnitude estimate of tinnitus is not made in isolation but is dependent on the interaction between three components: the tinnitus signal, the presence of contextual or background sound and residual factors. The tinnitus ALT is based on Helson’s (43) model of psychoacoustics.

Tinnitus is viewed as an auditory object and not merely as a sound signal, and the model adopts a holistic approach stressing active interaction between an individual experiencing tinnitus, cognition and their environment. The adaptation level (AL) is the body’s internal anchor or reference point (43). Any incoming stimulus is not processed in isolation but is compared to this reference for estimating sensory magnitude and making perceptual and discriminatory judgements. The final AL is the weighted mean of 3 components: 1) the focal component (tinnitus), 2) contextual stimuli (any background noise or applied sound therapy) and 3) residuals (individual cognitive or behavioural factors such as past experiences, prediction, emotion, personality traits, and physiological arousal. Attention and auditory scene analysis processes are weighting factors; the component which is attended to at any point in time will be given greater weighting and have increased influence in setting the internal anchor. An elevated internal AL is established for debilitating tinnitus, which is perceived as being of high magnitude and distress. Moreover, the adaptation level is determined by both present and past experiences of a stimulus and is able to change over time (43, 44).

It can be mathematically explained as:

\[ A = X^p B^q R^r \]

Where:

\[ p,q,r = \text{weighting factors (determine which components are given significance at any one time (p+q+r=1)} \]

\[ A = \text{Final adaptation level for tinnitus} \]

\[ X = \text{Tinnitus perception} \]

\[ B = \text{Background/contextual sound perception} \]

\[ R = \text{Residual factors} \]
Tinnitus audibility and severity have been hypothesized to vary with altering properties of individual residual effects (personality traits, emotion and prediction/anticipation of sounds).

In this PhD thesis a variety of theoretical (scoping review, narrative review) and experimental techniques (questionnaire/survey, behavioural studies, electrophysiological) were used to examine individual residuals. A randomized clinical trial was conducted to investigate the long-term effect of manipulating a particular residual on tinnitus outcomes. Seven studies were conducted in total.

10.1. Summary of Findings

The first study (Chapter 3) was a scoping review of existing current literature, in order to produce a coherent map of which personality traits are related to tinnitus perception and distress, and comprehend the relationship between tinnitus and affective disorders in adults. Sixty studies were chosen for charting the data. Fourteen studies examined personality traits exclusively, 31 studies examined affective disorders exclusively and 15 studies investigated both. Studies were predominantly cross-sectional in design using questionnaires. The majority of studies were conducted in Europe, and the age of participants was generally 40-55 years old. Personality traits of high Neuroticism, low Extraversion, high Stress Reaction, higher Alienation, lower Social Closeness, lower Well-Being, lower Self Control, lower psychological Acceptance, presence of a Type D Personality and externalized Locus of Control had a consistent association with tinnitus distress experienced by adult tinnitus help-seekers. Various studies often described similar underlying constructs using different terminology, or assessed the same construct using diverse scales. This can potentially confound searching results on scientific databases and be erroneous in interpretation. By mapping data together by similar themes, it was possible to see the emergence of four key traits pertaining to increased tinnitus severity: high Stress Reaction, low Social Closeness, high Alienation and low Self Control. There were contradictory findings reported in literature for whether depression and anxiety is more common among tinnitus sufferers (381-386). Again scoping all relevant data available allowed us to support the notion that anxiety and depression symptoms and/or disorders are more prevalent among the tinnitus clinical population and at elevated levels. However, it is difficult to judge the direction of this relationship due to the considerable overlap in presenting symptoms of psychological disorders and tinnitus. It is important to highlight that help-seekers are a subgroup and do not
form the entire tinnitus population. There are those with distressing symptoms who do not seek help as well persons with tinnitus but no distress. Tinnitus patients presenting at hospitals might be a subgroup of the larger general tinnitus population, with intense symptoms.

In Chapter 4, a web-based survey using relevant subscales of the Multidimensional Personality Questionnaire (MPQ) was administered in order to compare personality trait profiles between tinnitus sufferers and a comparison group of non-tinnitus individuals with hearing loss. Personality questionnaires are a highly valid and stable way of measuring personality traits, and the measured traits can remain stable over several years (49, 443). The full MPQ is a 278 item questionnaire, which has been extensively used due to its high resolution measure of personality, and has high internal reliability and high validity (48, 373, 437). Tinnitus sufferers had higher levels of stress reaction, lower social closeness, lower self-control and higher alienation than individuals with hearing loss and without tinnitus. These results were not confounded by the variables of age, gender and self-reported degree of hearing loss. The majority of respondents were aged 61 years or older: given that tinnitus occurrence and distress increases with age with the highest prevalence rate for tinnitus is observable in the 60’s and 70’s age group (11, 12) it is possible for mean distress levels to be heightened in this age group compared to the general population mean. Correlations between high stress reaction and self-reported tinnitus perceptual characteristics were found: they are more likely to seek several tinnitus treatments, have tinnitus made worse by loud sounds and hyperacusis tendencies. High alienation traits were correlated with high tinnitus pitch and hyperacusis tendencies. Stress reaction and alienation are also both related to the Negativity Emotionality factor, tying in with the influence of low valence on tinnitus discussed in Chapter 5.

The personality traits outlined appear to be moderating variables which directly influence tinnitus distress (53). The theory of signal detection provides an example of how this might occur – personality traits can manipulate the response criterion placement when any given level of a signal becomes perceived as tinnitus, and a natural lax criterion set by an individual’s underlying personality might mean that there is higher tendency to detect a tinnitus signal and to report it (166, 167). We propose that the four key traits examined in this thesis can act as ‘maladaptive’ personality traits which divert attention and processing resources towards tinnitus and prevent habituation/shifts in the ALT model (r weighting decreased, p weighting increased), resulting in an increased tinnitus AL under the ALT
framework (Figure 52). The neural mechanisms by which personality traits and tinnitus may potentially interact can be persistent co-activation and increased strength of neural connections between tinnitus sub-networks coding various tinnitus perceptual characteristics (4) and networks coding certain ‘maladaptive’ personality traits. The findings are useful as it is not fully understood why some individuals are capable of habituating and adapt to their tinnitus, while it is sustained in others (15-20% of the tinnitus population) (11-13). These studies strengthened the role of psychological affect on tinnitus magnitude.

Figure 52. The presence of ‘maladaptive’ personality traits – high stress reaction, high alienation, low social closeness and low self-control increase tinnitus AL weighting overall by reducing ‘r’ weighting and increasing ‘p weighting’ of tinnitus.

Chapter 5 was a behavioural study examining the effects of short-term auditory and visual emotional stimuli administration (varying along the dimensions of valence and arousal) on tinnitus outcomes. Low valence auditory stimuli led to higher tinnitus loudness ratings in males and females and higher distress ratings in males only; loudness matches of tinnitus remained unchanged. This effect was exclusive to stimuli presented in the same modality as the tinnitus. Neuroimaging studies support increased resting state connectivity between the limbic system and auditory cortex in tinnitus patients (57, 313, 314, 461) and altered emotional networks in tinnitus sufferers (462-464). These changes are additional to the changes related to aging/maturation and hearing loss itself (460). Based on current
neurophysiological models of emotion which incorporate reciprocal connections between the auditory cortex and amygdala (132, 133) the level of valence of emotional stimuli may modulate connectivity from the amygdala to the auditory cortex. Both the amygdala and auditory cortex are activated more in response to unpleasant sounds when compared to neutral sounds (453), and electrophysiological studies have shown faster response times to negative than positive stimuli (655). It is possible that in tinnitus sufferers, regions encoding unpleasant auditory stimuli become closely coupled (i.e. greater strength of functional connectivity established over time) with the regions encoding the tinnitus core network necessary for perception, and also general distress and salience networks. In order to better understand the neural networks activated upon short-scale exposure to emotional sound in individuals with tinnitus, further research using spatial imaging techniques such as functional magnetic resonance imaging (656) can be employed under similar paradigms. When modelled under ALT, the introduction of low valence sounds shift AL weighting in favour of external sound (increased q weighting), however, this effect is smaller than the increase in weighting of the tinnitus focal component via the residual pathway encompassing emotional affect (decreased r weighting, increased p weighting) (Figure 53). There would be a net increase in AL.

Chapters 6-8 investigated the role of auditory prediction under the ALT framework. The narrative review of Chapter 6 examined the feasibility of a relationship between auditory memory, predictive coding and tinnitus generation in the auditory system. The predictive coding model based on the Bayesian brain hypothesis, attention diversion and top-down feedback serves as the fundamental framework in current literature for how auditory prediction and sequential processing of auditory objects may occur (61, 68-70). This may rely on the presence of inhibitory neural templates within the auditory system (493, 494). Event-related potentials such as N1 or Mismatch Negativity are common electrophysiological indicators of predictive processes (280, 599). There are roughly equal number of studies providing for and against a relationship between the presence of tinnitus and specific changes in oscillatory band analysis (573), although persistent theta-gamma wave coupling activity has been associated with tinnitus conscious perception (67, 552). While there was theoretical
Figure 53. Short-term administration of low valence auditory stimuli increases AL weighting overall by reducing ‘r’ weighting’ and increasing ‘p weighting’ of tinnitus. The change triggered by the low valence characteristic of sound is greater than the effect of introduction of external sound.

and indirect electrophysiological evidence supporting the notion of tinnitus perception arising as a result of continuous topographically-restricted prediction error following missing auditory input (7, 67), there were few empirical studies which have directly tested this hypothesis. If proven correct, prediction-error driven changes among tinnitus sufferers may potentially explain global attentional disruptions, salience functional networks as well as theta-gamma coupling (gamma bands transfer prediction errors to higher-order regions, theta bands synchronize activity between different cortical sites) (4, 7, 67).

Chapters 7 and 8 subsequently empirically examined aspects of the hypothesis of topographically-restricted prediction error giving rise to tinnitus. The preliminary behavioural study and two-week feasibility trial outlined in Chapter 7 administered 30 minutes of Unpredictable and Predictable computer-generated surf sound administration to tinnitus sufferers. Both Unpredictable and Predictable sounds led to a decrease in tinnitus loudness, however, only Unpredictable led to a decrease in tinnitus distress ratings. Loudness level matches did not change. Under the ALT, this can be modelled as that the novelty presented in Unpredictable surf sound shifted attention, providing greater informational masking (171)
and allocation of global cognitive resources towards its processing (183, 624, 657); this creates a further facilitating effect for shifting AL away from tinnitus and towards external noise (Figure 54). Limitations which arose during the feasibility trial were that the computer-generated sound sounded static and was reported as not pleasant to listen to over long periods of time.

![Prediction (Short-term)
Novelty of Unpredictable Sound](image)

**Figure 54.** Short-term administration of Unpredictable sound presents the auditory system with greater prediction errors during processing compared to Predictable sound. This creates a facilitating effect in reducing AL weighting overall by increasing ‘r weighting’ and ‘q weighting’ and decreasing ‘p weighting’ of tinnitus. This effect is additional to the shift in AL away from tinnitus and towards external sound in general.

Chapter 8 was an electrophysiological study of whether auditory segregation streaming and predictive processing is affected in tinnitus sufferers compared to non-tinnitus controls with group matched level of hearing loss (similar level of peripheral deafferentation). The presence of tinnitus did not affect preliminary predictive auditory processing (within the first 100ms after onset). However, cortical-level auditory stream segregation may be disrupted among individuals with tinnitus at or near the frequencies corresponding to tinnitus pitch., observed as enhanced resting-state N1c and abnormal growth of N1c waveforms as frequency differences of stimuli increased. Disruption to auditory streaming processing can occur within the ambiguous region, in which attention or contextual alterations can bias perception towards either coherence or streaming (595, 596). This supports the hypothesis that
topographically-restricted prediction errors may be continually generated in tinnitus following peripheral deafferentation (7). This error, along with top-down feedback, tinnitus salient characteristics and conflict with expectations of sound can lead to tinnitus recruiting attention and cognitive resources during the later stages of object processing (5, 6, 78, 343). This in turn can compromise streaming segregation processing of external sounds. Under the ALT framework, attention and auditory stream analysis processing is increased towards tinnitus and residual (high prediction error) components, which increases AL tinnitus (Figure 55). This increase is greater than any shifts in AL towards the external sound played. There was no support in this study for differences in theta and gamma activity between tinnitus and controls.

![Image](attachment:55.png)

**Figure 55.** Due to salient features and constant prediction errors elicited by tinnitus, attention and ASA processing is increased towards tinnitus (‘p weighting’ increases) and residual (‘r weighting’ increases) components, overall increasing AL weighting. This effect is greater than any shifts in AL away from tinnitus and towards external sound played. This effect is also greater than any increase in residual or external sound weighting due to processing of prediction error within the external ABA sound stimuli (processing is disrupted).

In Chapter 9, a randomized clinical trial was undertaken. The trial incorporated the findings of prior studies. It tested the hypothesis that nature (Unpredictable) sounds, that are of higher valence and which hypothetically elicit greater prediction errors, will result in greater improvement of tinnitus impact of life (measured using TFI) and tinnitus-related outcomes
than neutral broadband noise (Predictable). Each sound was administered for 8 weeks each in a randomized cross-over fashion. Overall, the presence of sound had a positive effect on the TFI; however, this effect was primary driven by BBN sound therapy which resulted in a greater reduction of TFI than nature sound (slight increase in TFI at 8 weeks). The positive effect of sound on tinnitus was supported by secondary tinnitus (reduced loudness rating scale, reduced annoyance rating scale, reduced minimum masking level matches) and psychological-related outcome measures (increased positive emotionality, anxiety, depression and stress scores), but not interviews. BBN sound resulted in an increase in loudness level matches needed to match tinnitus. There was minimal change in loudness level matches for nature sounds. BBN and nature sounds did not differ significantly on changes in other tinnitus, emotion, attention and psychological state outcomes after 8 weeks of administration. The hypothesis that the novelty associated with unpredictable sounds will result in greater prediction error generation than predictable sounds was not held overall. There were indications of individual preferences and individual outcome effects observed. The presence of tinnitus subgroups was apparent in terms of which sound was most favoured, which sound had the most benefit, as well as in how sound-tinnitus interactions occurred as time progressed. A broader discussion of these results is presented in the “Clinical Implications for Sound Therapy Treatment” section.

Interpreted under an ALT framework, the findings from Chapter 9 suggest that internal AL weighting shifts away from the tinnitus signal and towards the sound therapy stimuli can occur over time (Figure 56). Direct increases in weighting placed on external sound may be driven via attention and auditory streaming shifts. This may involve recruitment of tinnitus core networks, the minimal set of brain areas that needs to be simultaneously active in order for tinnitus to be consciously perceived (4). However, another indirect tinnitus-residual-external sound pathway may also exist in which tinnitus is alleviated as a result of psychological benefit, potentially involving complex non-auditory networks such as the emotional, arousal, attention and memory (2, 78, 128, 204); forming a facilitating residual effect which reduces tinnitus severity.

The auditory system may adjust to sound therapy stimuli over time; this would eventually stop further AL shifts and result in shifts back towards tinnitus (5). Underlying loudness adaptation may occur through gain control, or adjustment of input-output sound functions of auditory neurons (e.g. decreases in neural spiking such that the increase in gain response levels off over time) (135, 320). Due to lack of novelty, Predictable sounds may undergo
loudness adaptation at a faster rate (sometime between 4 and 8 weeks after the first introduction of the sound) than Unpredictable sounds. Nature sounds due to their intermittent nature may take longer to reach peak adaptation. This is highly likely the reason for differing loudness level matches at 8 weeks as opposed to any intrinsic differences in tinnitus levels due to administration of the two sounds.

\[ A \downarrow = X^p \uparrow B^q \uparrow R^r \uparrow \]

**Figure 56.** Longer term administration of sound therapy results in a ‘presence of sound’ effect. AL weighing is reduced overall as a result of reduced ‘p weighting’ of tinnitus and increased ‘q weighting’ as AL shifts towards the external sound. A secondary ‘valence of sound’ effect may also occur via a tinnitus-residual-contextual noise pathway (due to psychological benefit of sound therapy), resulting in additional ‘r weighting’ increases.

**10.2. Adaptation Sensitive vs. Insensitive individuals**

The presence of different subgroups of tinnitus was observed with regards to tinnitus-external sound interactions, consistent with past studies in which tinnitus sufferers can have tinnitus
exacerbated by noise, exacerbated by quiet, or do not experience any changes to tinnitus with noise (10, 98). The heterogeneity of tinnitus poses an additional layer of complexity, with tinnitus subgroups that can vary based on pathophysiology, perceptual features, co-morbid conditions and treatment response (11, 98, 102, 189, 482, 658, 659).

Durai et al. (10) define individuals who were able to have tinnitus manipulated or not manipulated by environmental sounds as ‘adaptation-sensitive’ and ‘adaptation-insensitive’ persons respectively under the ALT framework. Differences in the ability to mask tinnitus with external sound has been used to classify individuals to subgroups in the past (113, 169).

Feldmann (42) defined a “resistance type” tinnitus in approximately 11% of participants which could not be masked. Some of these individuals could be more prone to having external influences play a role in magnitude judgment processing in general.

Using statistical analysis, Tyler (189) identified four, preliminary, subgroups of tinnitus:

1) Loud, persistent, and distressing tinnitus, accompanying hyperacusis
2) Tinnitus varying in pitch and loudness, and which is made worse in noise
3) Tinnitus eliciting low distress, no hyperacusis
4) Tinnitus which is worse in quiet and better in noise, low level tinnitus loudness which is not too distressing, no hyperacusis

Clinical trials of tinnitus treatments based on subgroups are needed. It is important in initial assessments to identify whether an individual falls into a particular subgroup, as there may be a common underlying physiological cause or presentation which can be addressed (342), counselling and sound therapy might be catered to suit the group, or the effects of clinical treatment can be monitored within a particular subgroup rather than within the whole population (where effects may be masked or lost). The Tinnitus Research Initiative (TRI) has developed an international database since 2008 to collect data on tinnitus patients undergoing specific treatments and who are assessed with standardized outcome measures (e.g. questionnaires, psychoacoustic matching) which enables for better delineation of the different subgroups (102). Next steps in research with ALT can perhaps involve modelling such extensive sets of empirical data to this framework using techniques such as computational modelling (134, 660), discussed in Section 10.5. Future Directions below.
10.3. Clinical Implications for Sound Therapy Treatment

The residuals of personality and prediction exclusively have not been included in clinical treatment paradigms to date (20, 35, 167, 368), although it is understood that psychological disturbances such as anxiety and/or depression often co-exist with tinnitus. The use of screening questionnaires such as the MPQ subscales in clinics may be useful in identifying at-risk individuals for distressing tinnitus based on personality profiles. Within the context of obesity as an example, specific personality traits such as high neuroticism and impulsiveness have been identified as high risk factors (445). Within at-risk subgroups, personalized treatment options (e.g. psychoeducational or psychotherapeutic techniques) may be administered. Similarly, the presence of specific personality traits when measured on a personality questionnaire may act as early markers for tinnitus susceptibility or severity over time. If an individual is able to gain an internal locus of control over their tinnitus through training (e.g. through instruction, reward/punishments or understanding the stimuli) (446), this might possibly shift the internal criterion for tinnitus detection over time. Further research would therefore be beneficial in this area.

Emotion as an individual residual factor is already considered clinically, and any informational counselling is highly likely to involve discussion around how negative emotions can exacerbate tinnitus. Based on the findings of this thesis, in individuals who are found to benefit from sound therapy, sound stimuli should be selected which are rated by the user as being neutral or of high valence (5 or above on a valence rating scale). This will enable for a facilitating effect in shifting AL away from tinnitus via the residual pathway, and provide psychological benefit during sound therapy. This would also prevent the evoking of negative reactions and exacerbation of perceived tinnitus loudness and distress. Moreover, valence ratings for sound stimuli should be taken as a function of sound loudness growth as well: it is possible that for steeply increasing loudness curves, negative reactions can be triggered at high volumes (23). Gradual blending of sound with tinnitus will allow for smooth AL shifts. Also, users can be advised to avoid environments in which they may be exposed to adverse sounds which can exacerbate tinnitus (e.g. noise pollution, traffic noise). It is possible for sounds to change in valence levels over time (55, 452), therefore valence ratings can be re-taken at regular follow-up appointments.
It is important to also maintain the novelty presented by sound therapy stimuli, such that prediction errors are continually elicited (7), the auditory system does not adapt to the sound quickly (36, 353, 354), and/or the continuity illusion is not elicited over time whereby context and predictions of most likely stimuli are utilized by auditory processing mechanisms to ‘fill in the gap’ in cases of intermittent masking (485). Alternating administering BBN (effective in terms of shifting attention away from tinnitus; reducing tinnitus impact) for a period of 6-8 weeks with nature sounds for a period of 6-8 weeks (preventing adaptation, eliciting prediction errors over time) may be advantageous (BBN-nature-BBN-nature...); however, more research is needed in this regard. Davis et al. (588) observed more consistent benefit over 12 months if Neuromonics Tinnitus Treatment involved masking of tinnitus for the first two months followed by intermittent perception of tinnitus compared to where there is intermittent perception of tinnitus throughout treatment. Also use of sounds that gradual fade in volume when “turning off” may reduce attention towards tinnitus, preventing or delaying tinnitus from coming back at full intensity.

It is useful clinically to present a variety of options to individuals for sound therapy, rather than a "one sound fit all approach" as although both BBN (same sound administered to all) and environmental (participants selected one sound from three) resulted in small but significant tinnitus and tinnitus related outcome improvements, in the interviews self selected sound was more relaxing and pleasant to listen to, and general wellbeing was increased in line with the holistic approach taken by ALT. For each sound stimulus administered, individual ideal treatment sound levels should be set based on tinnitus and sound loudness and annoyance, as discussed in the “Modelling of Sound under ALT” section below.

Another consideration based on study findings is that predictive regularity processing in normal auditory stream segregation may be disrupted in individuals with tinnitus. Within the context of everyday life, this can translate into difficulties in separating out different sound sources in noisy situations (e.g. following a stream of conversation in noisy environments). Errors in simultaneous grouping results in blending of sounds that should be heard as separate (69), and this blending can distort characteristics (e.g. frequency, quality or timbre) of incoming sounds. It would therefore also be useful to provide additional counselling and/or teach individuals with tinnitus strategies for coping with hearing in complex environments, similar to techniques taught for hearing loss, such as facing the person, reducing distance between speaker and themselves, etc.
In terms of clinical measurement, our study findings support the interpretation formed by some past studies (6, 10) that loudness level match changes as a measure is complicated by sound stimuli undergoing loudness adaptation as well. This might occur to a greater extent than tinnitus adaptation. Often in tinnitus treatments, significant subjective changes in tinnitus are present but with negligible objective loudness changes of tinnitus (39). Under the ALT, subjective loudness ratings and LLMs are distinct constructs which may utilise different reference points (6). Tinnitus LLMs are matched against an external sound (susceptible to change) as a reference point, while subjective loudness ratings are made in silence (constant over time). The final magnitude of tinnitus measured with ALT, encompassing various higher-order psychosocial factors and combining attributes of loudness, severity and tinnitus awareness (6, 158) may be a more realistic estimate of intervention outcome than psychoacoustic matches alone.

There was no correlation between quantitative tinnitus outcomes and the reported improvement of tinnitus by participants during interviews in this study. This highlights the discrepancies between quantitative and qualitative tinnitus measures. While the drawback may exist in that interviews are more prone to reporting bias than quantitative measures (652), the inclusion of interviews may be advantageous in obtaining detailed views of real life and influencing environmental factors (e.g. illness, stressful life events) which can affect long-term compliance of use and psychological benefit (653); therefore these measures should be readily incorporated into tinnitus treatment. It is also strongly advocated that the use of sound clinically should be in addition to (not instead of) counselling. As the results suggest, sound therapy involves more than passive exposure to sound, and participants need to be informed of this, and counselled also about how to use any sound administered.

10.4. Modelling of Sound under ALT

Based on the trial findings, it is possible to extract some features of an ideal sound therapy stimulus that may be preferred by users for sound therapy. An ideal sound therapy stimulus will steeply decrease perceived tinnitus loudness and annoyance as noise level is increased; loudness and annoyance function of the sound stimulus itself should increase very gradually with level. This will enable AL weighting to shift effectively from tinnitus towards the background stimulus, as well as allow greater “room” for adjustment for comfort, user preference, etc. A steep increase in sound stimulus can elicit distress, which may activate the
limbic and autonomic systems and increase tinnitus perception instead (196). Theoretically, therapy sounds which reach EL at a lower % of total sound level and reach EA at a higher % of total sound level are preferable as this would signify rapid changes in tinnitus characteristics following gradual increases in sound, without the possibility of the sound becoming too loud and/or evoking negative reactions itself. Moreover, in order to be effective, Searchfield et al. (5) have suggested two criterion for therapeutic sounds: 1) Sounds should be at low level below the tinnitus, so as to displace adaptation to tinnitus in the direction of the therapeutic sound, and 2) Sounds should be paid attention to. Therefore it is crucial that the level of therapeutic sound stimulus does not exceed the perceived loudness of tinnitus during administration. On the other hand, if stimuli are presented at a level considerably lower than Equal Loudness Level, they may have insufficient interaction with tinnitus to induce any shift in its AL. Sound levels for the trial in Chapter 9 were initially set one step (10%) below Equal Loudness Level and if participants preferred it to be slightly higher or lower due to comfort reasons, the sounds were further adjusted in order to stop evoking negative response. The final sound setting was therefore at a level where sound interfered with tinnitus perception but which is also comfortable for the user. These are considerations which need to be incorporated in clinical practice of sound therapy.

The Equal Annoyance Level and Equal Loudness Level can theoretically serve as good indicators of tinnitus loudness AL and distress AL at a given point in time. However the accuracy of these indicators to track changes in tinnitus clinically over time might be confounded by the fact that therapeutic sound can undergo sound adaptation as well (21).

10.5. Limitations and Considerations

10.5.1. Limitations of Current Studies and Future Considerations

This section discusses the limitations and challenges encountered while conducting the studies in this thesis. Suggestions are provided for how future studies related to the ALT may be shaped.

For the personality web-based survey (Chapter 4), it was initially expected that there will be 400-600 respondents. The final respondent count was considerably lower, with 154 tinnitus respondents and only 66 respondents for the non-tinnitus control group. The survey was open for 5 months. If greater time and financial resources were available, the survey may have
been open for a longer time and the number of respondents may have been greater. Also, in the future it would be of interest to compare individuals with tinnitus to those with other distressing, intractable conditions (e.g. chronic pain sufferers) to further isolate the effects exclusively related to tinnitus.

The emotion behavioural study (Chapter 5) used the IAPS and IADS stimuli, which have been specifically developed for experimental measures of emotion (448, 449). Each stimulus was 6 seconds long in duration, and the stimuli sets ranged from very high positive valence to negative valence. Ethical considerations were critical when designing and implementing this study, in order to avoid any harm to the participants. These imposed limitations on the study design, e.g. the duration of time to which participants may be exposed to negative, unpleasant stimuli. To better understand neural networks activated, further research using spatial imaging techniques (e.g. functional magnetic resonance imaging) might be useful. Also, it might be interesting to see if the introduction of a new audio-visual condition (congruent sounds and images) would result in an additive effect to single modality stimuli.

A considerable amount of time was spent in determining what would be the best way to measure prediction and tinnitus objectively, and also in subsequently adapting the deviation and omission paradigms to tinnitus for the electrophysiological study (Chapter 8). Due to the frequency span of test stimuli, the maximum tinnitus pitch of those who took part in this study had to be 8 kHz. This was a limitation of measurement software. Initially, it was also of interest to examine working memory capacity of tinnitus sufferers compared to controls. However, literature searches showed extensive work had been conducted in this area and this task was dropped. Future research may examine longer-term streaming and whether streaming segregation processing may be trained in individuals with tinnitus; also, whether training to re-categorize tinnitus as a real auditory object (thereby completing the hypothetically disrupted auditory streaming) would be advantageous.

The randomized controlled trial (Chapter 9) used sound therapy stimuli which did not compensate for hearing loss. Threshold adjusted noise (233) is implemented by several manufacturers of tinnitus aids (e.g. Siemens, Phonak, Oticon). The use of such adjustments may allow for delivering of sound therapy that would interact more with an individual’s tinnitus based on the pattern of hearing loss. The mode of administration (via MP3 players) may have also contributed to the lower percentage of perceived benefit reported by participants in the trial, compared to other studies (28, 32, 197, 622, 650). Future studies can
look at apply the findings obtained with regards sound selection and sound levels described here using more customized modes of administration, e.g. tinnitus aids which can stream BBN and nature sounds. Linking the aids to smartphones or tablet computers can allow for individuals to access a broad variety of therapeutic sounds.

Another drawback of current findings is that the factor of time is limited. In order to examine how administration of the proposed sound therapy affects long-term tinnitus, and to see if sound therapy effects are more robust than the susceptibility of tinnitus neural networks themselves to change over time (88, 468), longitudinal studies of tinnitus treatment over a long period of time (e.g. case studies followed over at least a year) are needed. Tinnitus loudness and distress also undergo different patterns of change over time: for example, if the tinnitus duration is less than 12 months, it tends to be low in loudness and high in annoyance but if tinnitus is present for more than 5 years, the opposite was seen with the tinnitus increasing in intensity but becoming less annoying (20, 181, 182, 661). Longitudinal study designs have been given insufficient focus in the current tinnitus literature (662). Weekly or monthly monitoring of outcomes would give a fine-scale representation of change over time. This will also counteract for the fact that short-term trials including a large group can mask individual differences arising due to tinnitus heterogeneity (663). Imaging techniques such as resting state fMRI with high spatial resolution model neural network changes over time (57, 464) and can be incorporated into measures alongside typical quantitative and qualitative intervention outcome measures.

Beyond the scope of this thesis was the investigation of attention as a weighting factor as well as ALT modelling of ideal sound therapy levels. The role of attention in tinnitus has been examined in depth in literature (158, 333-336). While attention is integral to several of the processes examined throughout this thesis (e.g. auditory streaming segregation, predictive processing, sound therapy) it remains difficult to control for attention exclusively. It remains possible that attentional shifts during testing can also shift the weighting placed on different ALT components, in addition to any experimental manipulations administered. However, the fact that data was collected on groups of individuals may complicate individual transient attention changes.
10.5.2. Significance and Validity of the ALT model

From the theoretical ALT framework, this thesis has allowed for empirical assessment of various individual factors which may contribute towards tinnitus perception and distress and sound therapy outcomes. Preliminary evidence shows support for the ALT framework and forms a good starting point; however, replicability of trials with larger sample sizes and consideration of the time factor is needed. This is a working model, with the possibility of future studies resulting in considerable changes and/or disproving of the framework. The residual factors are modelled to the ALT framework with the intention of coherently mapping all of the findings; it is acknowledged that alternative interpretations may be possible. As further studies are conducted, this framework will be made more specific for tinnitus.

The residuals examined in this thesis are intrinsic to the individual. It is acknowledged that the definition of residuals (individual cognitive and psychological factors) can encompass various other influences that are not part of the ALT framework. The inclusion of infinite residuals however would make the model unmanageable. It is argued to be more useful to extract key individual influences which interact in predictable ways to establish a final tinnitus magnitude. The residuals which are examined in this thesis were those already conceptualized in the ALT model for tinnitus as being relevant and feasible for tinnitus and tinnitus-sound interactions (5).

To obtain optimal sound levels, other residual variables should also be computed into this formula. Further research such as using computational models with several data (102, 134, 649) can enable for ideal sound therapy levels to be identified as well as for computing "automated" changes in level accordingly based on any changes in residuals or sound adaptation in the future, as discussed in the next section.

10.5.3. ALT and computational modelling

Considering tinnitus heterogeneity and individual variability, it becomes critical that models that take a holistic approach and that cater for multi-faceted influences on tinnitus, such as the ALT model, be considered more in research. The ALT is advantageous over some other tinnitus models as it is conceptualized using a mathematical model, which is able to be solved using methods of multiple linear regression analysis and least-squares (5). It is unlikely to be
a perfect model but it does enable for the effect of one component to be analysed while
controlling others. Searchfield et al. (6) suggest that a combination of theoretical,
experimental and computational models (a principles of systems physiology) approach can be
beneficial when applied to tinnitus, as it will better allow for examining long-term treatment
effects, identifying success and failure factors of treatment and deeper insights into the
interaction of individual neuropsychology with the environment and pathophysiology.

In order to delineate subgroups and predict how an individual might respond to potential
treatments, a computational model of ALT can be developed for use in initial assessments.
Computational modelling integrates mathematics, physics and computer science to study the
behaviour of complex systems by computer simulation (134, 660). Measurements of different
variables which can influence tinnitus as outlined in this thesis (for example, net effect of
residuals (R and r weighting), contextual sound levels (Q and q weighting), tinnitus
characteristics (P and p weighting), as well as demographic factors such as gender, age,
degree of hearing loss, attention and auditory streaming thresholds as additional weighting
factor influences) can be imputed and simulations run by adjusting each variable to compute
an individual’s predicted intervention outcomes (final tinnitus AL level). Within the context
of sound therapy, for example, a final AL estimate that is lower than current AL levels will
indicate the treatment will alleviate tinnitus; no change in AL will correspond with no
anticipated change in tinnitus and an increased in AL estimate will mean tinnitus will become
exacerbated. In tinnitus research, computational modelling has been applied in the study of
mechanisms giving rise to tinnitus, in which it was concluded that lateral inhibition,
homeostatic plasticity, and gain adaptation could all in principle be involved in generating
tinnitus-related neuronal activity patterns (134). The computational model of ALT will be
based on accumulation of tinnitus empirical data and databases to date. The findings from
this thesis can form a basic computational template to build-on. One illustration would be if
the individual has high maladaptive trait levels measured present (including high stress
reaction and low self control) coupled with exacerbation of tinnitus with sound, this would
stop a clinician from administering sound therapy due to contraindications (20) and
psychological-based interventions may be allocated as first preference (234, 237, 427).

An example of a computational model recently developed for tinnitus generation following
homeostatic neuroplasticity is the neural oscillator and a neuronal network model (649)
(Figure 63). This consists of two layers of excitatory neurons (A and B), one layer of
inhibitory neurons (C) and coupling weighting factors (W). The effect of changing input into
any one component is clearly defined by weighting factor changes and final output change. A completed computational model of ALT will eventually have defined coupling weightings and relationships between the various components (connecting lines) established.

**Figure 57.** Example of a computational network model for tinnitus generation consisting of two layers of excitatory neurons (A and B), one layer of inhibitory neurons (C) and coupling weighting factors (W).
Chapter 11. Conclusions
Based on the results of this doctoral thesis, residuals of personality traits, emotion, memory and prediction may each individually contribute towards determining final tinnitus magnitude under the ALT model of tinnitus perception. Four key personality traits of high stress reaction, low social closeness, low self-control and high alienation were consistently present in association with tinnitus severity, and also significantly differed in levels between individuals with tinnitus and those without tinnitus but matched for age, gender and hearing loss. Transient exposure (in the time span of a few minutes) to unpleasant auditory stimuli resulted in exacerbation of tinnitus. Predictive error coding in auditory memory can theoretically generate tinnitus perception, under a Bayesian brain model. Short-term (in the span of several minutes) exposure to Unpredictable sounds affected tinnitus perception more than Predictable sounds. Using electroencephalography methods, disruption to auditory streaming segregation processes was observed among tinnitus sufferers at sites corresponding to pitch of tinnitus. This may be explained by a depletion of attentional resources for processing external sound, which are instead directed towards constant topographically-restricted prediction errors arising due to missing auditory input. Administration of sound therapy (broadband noise; nature sounds) in general had a positive effect on tinnitus impact. This was supported by various secondary tinnitus (reduced loudness rating scale, reduced annoyance rating scale, reduced minimum masking level matches) and psychological-related (increased positive emotionality, anxiety, depression and stress scores) outcome measures, but not interviews. Different sound therapy stimuli may work by biasing weighting along these pathways. Individual variability was present in response to sound therapy and preference of therapeutic sound; the presence of tinnitus subgroups was also evident.
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