



Background to Tinnitus Treatment

In a widely recognized authoritative text on Tinnitus, Baguley et al (Tinnitus: A Multidisciplinary Approach, Blackwell Publishing 2013) promotes Tinnitus management strategies built upon collaborative care from the fields of audiology, otology, psychology, psychiatry and auditory neuroscience. Most researchers and clinicians report that a combination of sound therapy and counselling facilitates the patient's ability to manage their Tinnitus experience.

Research over the last 20 years has moved on from the primary focus for Tinnitus pathogenesis being the ear to now include the central auditory pathways of the brain and other nonauditory neural systems, particularly the limbic, autonomic and reticular systems. To understand and describe the mechanisms of Tinnitus it is necessary to make distinction between the ignition point of a Tinnitus, ie the most peripheral point at which the activity is generated, and those promoting mechanisms that ensure that the Tinnitus is prioritized by auditory and attentional systems within the brain.

A common ignition point for noise induced Tinnitus, the primary target for the Aurex-3 development, occurs within damaged areas of the fine tonotopic structures of the cochlea or inner ear. At its heart is the Organ of Corti, a complex structure whose micromechanical properties allow the transduction of sound. This is accomplished by 15,500 hair cells, these being arranged tonotopically and being innervated by 30,000 afferent nerve fibres. Of the two types of hair cell in the cochlea the inner hair cells form a single row of 3,500 and the 12,000 outer hair cells are arranged in three rows.

Calcium transport is an important factor in the functioning of the cochlea (Patuzzi, R Ion flow in cochlear hair cells and the regulation of hearing sensitivity, Hearing Research, 280, 2011). The stereocilia of inner and outer hair cells are surrounded by endolymph, a high potassium/low sodium fluid. The base of each hair cell is surrounded by perilymph, a low potassium/high sodium/high calcium solution. Incoming sound sets up waveforms which displaces the hair cell stereocilia from their resting position. This mechanical change results in the opening of ion channels on the stereocilia, allowing potassium to enter the hair cells, changing the electrical potential and thereby causing voltage gated calcium channels to open. In inner hair cells this results in neurotransmitter release leading to activation of the auditory nerve.

For Tinnitus to be a conscious perception of sound there must be a representation of that sound within the auditory brain. The effect of cochlear dysfunction on auditory pathways is unclear. Experimental evidence supports that there are multiple possible mechanisms for Tinnitus generation, occurring at all levels of the auditory pathways. The ignition point of the Tinnitus maybe in the auditory system, but interaction with the limbic system performs an inhibitory role. Failure of this 'noise cancellation system' may be a cause of Tinnitus (Leaver et al. Dysregulation of limbic and auditory networks in tinnitus, Neuron, 69, 2011).

The accepted neurophysiological and psychological models of Tinnitus suggest that although peripheral otological disease may trigger Tinnitus, central auditory processes and related systems of reaction and emotion are more important in the distress and long-term effects of the symptom.

Although Tinnitus is one of the most common physical symptoms to affect humanity, it continues to pose challenges to clinicians and researchers alike. In large measure this is because the effects of Tinnitus are so variable and the impact of Tinnitus ranges from little or nothing to profound and life changing. Tinnitus has been associated to varying degrees in different individuals, with changes in thinking, stress arousal, mood, sleep and behavior and with auditory interference. These changes in turn may lead to other behavioural and psychological consequences.

The Aurex psychophysics model and its differentiation from currently available treatments for Tinnitus

Many therapeutic options have been considered in the management of Tinnitus, including surgical treatments, drug treatments, psychological techniques and physical therapies. Many are still practiced though often the evidence base is weak or completely lacking.

Sound therapy for the relief of Tinnitus is not new, dating back as far as ancient Babylon in 650 BC. The use of Tinnitus maskers was pioneered by Vernon in the 1970's (Vernon, J., Attempts to relieve tinnitus, *Journal of the American Audiology Society*, 2, 1977).

In the USA, Henry and colleagues (Henry, J.A, et al Using therapeutic sound with progressive audiologic tinnitus management, *Trends in Amplification*, 12, 2010) introduced a framework for the management of troublesome Tinnitus to the USA Veterans Administration, Progressive Tinnitus Management, in which sound therapy is an essential component derived from combinations of sound and types of sound to manage Tinnitus.

The underlying principle used in the Aurex-3 considers the extent to which amplitude modulation of a stimulus will increase the acceptability and efficacy of sound therapy for a patient. In particular the synthesis of a complex sound signal from the intermodulation of two variable frequency generators and their combined amplitude modulation is used to generate a complex harmonic spectrum that is user controlled to match the patient's Tinnitus sound. Furthermore, the introduction of beat harmonics is used to specifically excite the areas of a patient's Tinnitus sound derived from neurophysiological and psychological dysfunction. This is a unique and patented aspect of the Aurex-3 modality.

The beat harmonic excitation is applied conductively to the cochlea and counterintuitively creates a consonant and hence relaxing effect. The resultant relaxation to create a soporific effect offers respite to the patient and encourages continued use. Relaxation has often been included as an element of other treatment approaches (Dineen, R. et al Managing tinnitus: a comparison of different approaches to tinnitus management training, *Brit. Journal of Audiology*, 31, 1997).

Regular and continued use of the Aurex-3 matched to a patient's Tinnitus sound in this way acts to reverse the psychological 'repetitive memory function' of Tinnitus by neuronal plasticity together with cognitive reprocessing.

The 'Aurex' effect

Central to the Aurex-3 approach is the application of beat harmonics.

Traditionally, dissonance has been widely believed to be the product of "beating": interference between frequency components in the cochlea that has been believed to be more pronounced in dissonant than consonant sounds. However, harmonic frequency relations, a higher-order sound attribute closely related to pitch perception, has also been proposed to account for consonance. Some combinations of musical notes sound pleasing and are termed "consonant," but others sound unpleasant and are termed "dissonant." The distinction between consonance and dissonance plays a central role in Western music, and its origins have posed one of the oldest and most debated problems in perception.

Contemporary thinking on consonance is instead rooted in acoustics, beginning with the fact that musical instrument and voice sounds are composed of multiple discrete frequencies. These frequencies are termed "harmonics" because they are typically integer multiples of the fundamental frequency of the sound. Harmonics are combined in a single waveform when traveling in the air but are partly segregated by the cochlea, because different auditory nerve fibers respond to different frequencies (Plomp, R. The ear as a frequency analyzer, *J Acoustic Society America*, 36, 1964).

When several notes are combined, the resulting sound waveform that enters the ear contains all of the individual frequencies of each note. Auditory scientists have long noted that aspects of the pattern of component frequencies differ between consonant and dissonant chords. Prevailing theories ascribe consonance to the fact that dissonant chords contain frequency components that are too closely spaced to be resolved by the cochlea. Two such components shift in and out of phase over time, producing an interaction that oscillates between constructive and destructive interference. The amplitude of the combined physical waveform thus alternately waxes and wanes. If the components are close enough to excite the same set of auditory fibers, amplitude modulations are directly observable in the response of the auditory nerve. These amplitude modulations are called “beats,” and result in an unpleasant sensation known as “roughness,” analogous to the tactile roughness felt when touching a corrugated surface [in practice, the perception of roughness is dependent on the depth and rate of amplitude modulation, as well as the center frequency of the tones involved. Theories of dissonance based on beating have been dominant in the last century and are now a regular presence in textbooks (Deutsch, D., *The psychology of music*, Academic, San Diego, 2009).

However, a second acoustic property also differentiates consonance and dissonance: the component frequencies of the notes of consonant chords combine to produce an aggregate spectrum that is typically harmonic, resembling the spectrum of a single sound with a lower pitch. In contrast, dissonant chords produce an inharmonic spectrum. Such observations led to a series of analyses and models of consonance based on harmonicity (Ebeling, M. Neuronal periodicity detection as a basis for the perception of consonance, *J Acoustic Society America*, 12, 2008) Although beating-based theories are widely accepted as the standard account of consonance, harmonicity has remained a plausible alternative. Mc Dermott et al (Mc Dermott, JH, et al, Individual differences reveal the basis of consonance, *Curr Biol*, 20, 2010) argues that harmonicity is more closely related to consonance than is beating.

This disassociation of harmonicity from beating in the Aurex-3 and its unique matching to a person's Tinnitus sound presents a unique and differentiated model and modality for Tinnitus treatment.