Whitepaper

Customized Sound Therapy During Sleep:

An Optimal Pathway to Care for Patients Suffering from Tinnitus.

This document is the first, in a four-part whitepaper series where the tinnitus pathogenesis and the unique approach that Levo Medical has taken in its therapy is evaluated. Please consult www.levomedical.com for further information on our FDA-cleared, scientifically proven, and effective therapy.

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Glossary of Terms

TFI - Tinnitus Functional Index

THI - Tinnitus Handicap Inventory

Sound Pressure – The pressure deviation of a sound wave from the ambient expressed in Pascals (Pa)

Sound Pressure Level – Effective sound pressure relative to a reference (usually the threshold of human hearing) and it is expressed in decibels (dB)

Sound Loudness – Subjective perception of Sound Pressure

Sound Volume – Sound Loudness

Part 1

Tinnitus – What Is It and How Does It Develop

Subjective Tinnitus is the phantom perception of sound with no external source. It is believed to originate from abnormal, spontaneous neural activity in the brain's auditory pathways and auditory cortex. *Of the roughly 50 million people who have tinnitus in the USA, around 10 - 12 million of them report it as being bothersome enough to warrant seeking help* (Jarach, 2022; Audiologic Guidelines for the Diagnosis and Management of Tinnitus Patients, 2001). Habituation (diminishing the response) to this phantom sound occurs naturally in 50% of cases (Hesse, 2006). When habituation does not occur, tinnitus results in concentration problems, depressive symptoms, and sleep disturbances. Despite the rising prevalence and significant impact of tinnitus, there remain gaps in care for these patients. Audiologists and other hearing care providers are the best suited and best positioned healthcare professionals to provide tinnitus services, but relatively few do so. Currently, tinnitus care across clinics is highly variable, not evidence based, and lacks standardized measurement of outcomes (Henry, 2019).

Neuroplasticity and Tinnitus

Our brain has the amazing capacity to reorganize itself, both in structure and function by changing the way our neurons are connected and even recruiting or generating new neurons. This capacity is known as neuroplasticity and is responsible for our ability to learn, adapt and adjust to changes such as lesions. However, this process sometimes does not function as expected. Tinnitus may be the result of neuroplasticity mediated changes that develop because of decreased input from the ear, deprivation of sound stimulation, overstimulation or yet unknown factors and coupled with neuronal changes in auditory and extra-auditory brain networks (Jastreboff, 1990; Henton, 2021). In most cases, damage to outer hair cells in particular cochlear regions results in less neural input, which the brain counteracts by increasing excitation and response gain (Eggermont, 2004). As a result, an increase in spontaneous firing rate in the neurons involved may happen at different levels of the auditory pathways (Noreña, 2003; Schaette, 2009). Because the brain is not able to discern if this abnormal incoming flux of information is related to real environmental sound, a 'phantom sensation' (tinnitus) may be created similar to other phantom percepts such as phantom limbs or auditory hallucinations (Jastreboff, 1990; Hanton 2021). Regardless of its peripherical lesion-related trigger, tinnitus arises in the central nervous system.

There is good news. The neural plastic mechanisms that facilitated the changes can be leveraged to reverse them (Schaette, 2006). By increasing auditory nerve activity with proper acoustic stimulation, tinnitus volume can be reduced (Schaette, 2009).

Tinnitus Management Using Sound Therapy

Sound stimulation may provide immediate relief by lessening the perception and producing long-term reduction of tinnitus. This may be achieved through the induction of changes mediated by neuroplasticity that can lead to habituation. (McKenna, 2004). Methods of sound stimulation may be classified into two groups: customized vs non-customized.

A. Customized sound therapy (CST) is a strategy based on the individual's tinnitus symptoms and sound characteristics. The aim of CST is to facilitate neuroplasticity mediated changes and reorganization of the auditory processing network by restoring the inhibitory/excitatory balance for long-term benefits. Therefore, CST seeks to reprogram the brain to achieve a reduction of sound loudness and a desensitization to tinnitus. It includes a wide range of therapeutic approaches among which stand out (a) tinnitus pitch-matched therapy; (b) tailor-made notched music training; (c) Heidelberg neuro-music therapy; (d) acoustic coordinated reset neuromodulation therapy and (f) modulated wave therapy and. It is widely agreed that customized sound stimulation has a better tinnitus-suppression effect than non-customized sound. (Schaette, 2010; Theodoroff, 2017; Mahboubi, 2017; Wang, 2020).

B. Non-customized sound therapy (NCST) uses unmodified noise, music, or environmental sounds as stimulating sounds and seeks to improve the adverse physiological and emotional reactions associated with tinnitus by masking the tinnitus or helping patients become accustomed to the tinnitus. (Vernon, 1976; Vernon, 1977; Jastreboff, 1995; Wang, 2020). Examples of this approach are total and partial masking therapy, and hearing aids.

Customized sound therapy treatments performed using the frequency content of the perceived tinnitus are intended to induce plasticity changes able to reverse the previous misled plasticity changes that caused tinnitus (Han, 2019). Scientific evidence published in the last two decades states that there is a strong relationship between the spectral characteristics (frequency content) of tinnitus and the site of the cochlear lesion that originated it. The "edge theory" for tinnitus pathogenesis suggests that tinnitus can be the result of an increase in the inner ear´s hair cells activity of the edge regions of a cochlear lesion (Haider, 2018). The best therapeutic outcomes for CST are obtained when the sound stimulation encompasses some of the spectral and/or intensity characteristics of the tinnitus (Schaette, 2010). Incorporating the tinnitus pitch and/or range of hearing loss frequencies has been shown to be particularly effective in reversing the development of tinnitus-related neural hyperactivity (Noreña, 2006; Schaette, 2006).

The Levo System

The LEVO system takes customized sound therapy to the next level by using a precise sound match of the perceived tinnitus and applying the sound during sleep.

The Levo system is made up of two parts, the Levo Manager that runs on the physician's iPad and a separate software that runs on the patient's iPod touch. The system allows the therapists to create a sound that closely matches the spectral and intensity level characteristics of the perceived tinnitus and upload the sound to the patient's device. Patients can set the intensity level of sound stimulation every night and the system automatically stores all the stimulation data daily. Customized high quality in-ear earbuds deliver precisely calibrated sound in the range 0.125–16 kHz and are especially designed for comfortable sleep use. The sound that Levo delivers provides highly precise customized acoustic patterns that significantly increase the ability to reprogram the brain to reverse the changes that caused tinnitus (Pedemonte, 2010). Using a sound that precisely matches the patient's perception has additional advantages: (1) it provides a way of performing a controlled exposure to the tinnitus sound with the emotional "shelter" of being within a therapy protocol; (2) it provides psychological relief since the patients realize that their tinnitus is reproducible and understandable by others; (3) it has a relaxing effect, because during the stimulation the patient hears the sound coming from outside and stops hearing it in their head or ears.

Each night the patient goes to sleep using the Levo System. Levo System easily allows the user to adjust the sound level of each or both ears to match the tinnitus' perceived sound volume on that same night.

Additionally, Levo's calibration precision and its ability to store data from each night of stimulation allows to graphically display the evolution of tinnitus intensity throughout the treatment. This chart is extremely useful for the evaluation of the patient's progress and gives the patients psychological reinforcement through treatment. Changes in intensity observed during treatment with the Levo system have shown a high correlation with improvement in widely accepted psychological tests scores such as Tinnitus Functional Index, Tinnitus Handicap Inventory and Tinnitus Reaction Questionnaire (Drexler, 2016).

Levo Protocol

The therapy lasts 9 months divided into two phases ("continuous stimulation" and "detachment") that are preceded by an adaptation period as shown in figure 1.

The adaptation period is patient specific and can last up to 1-2 months but can also be as short as 2-3 weeks. At this stage, the patient learns to use the device, is trained in adjusting the therapy sound level for each night and learns to sleep with it.

Once the patient has adapted, the two phases of therapy begin:

- The "continuous stimulation" phase that lasts between 3 and 6 months in which the patient uses the device every night. During this phase, the intensity of the tinnitus tends to decrease until it reaches a lower plateau.

- The "detachment phase" allows the patient to begin to detach from the treatment. In this stage, the days per week of stimulation are progressively reduced and the patient no longer uses the device on a regular basis. This phase lasts approximately 3 months and can be extended if needed.

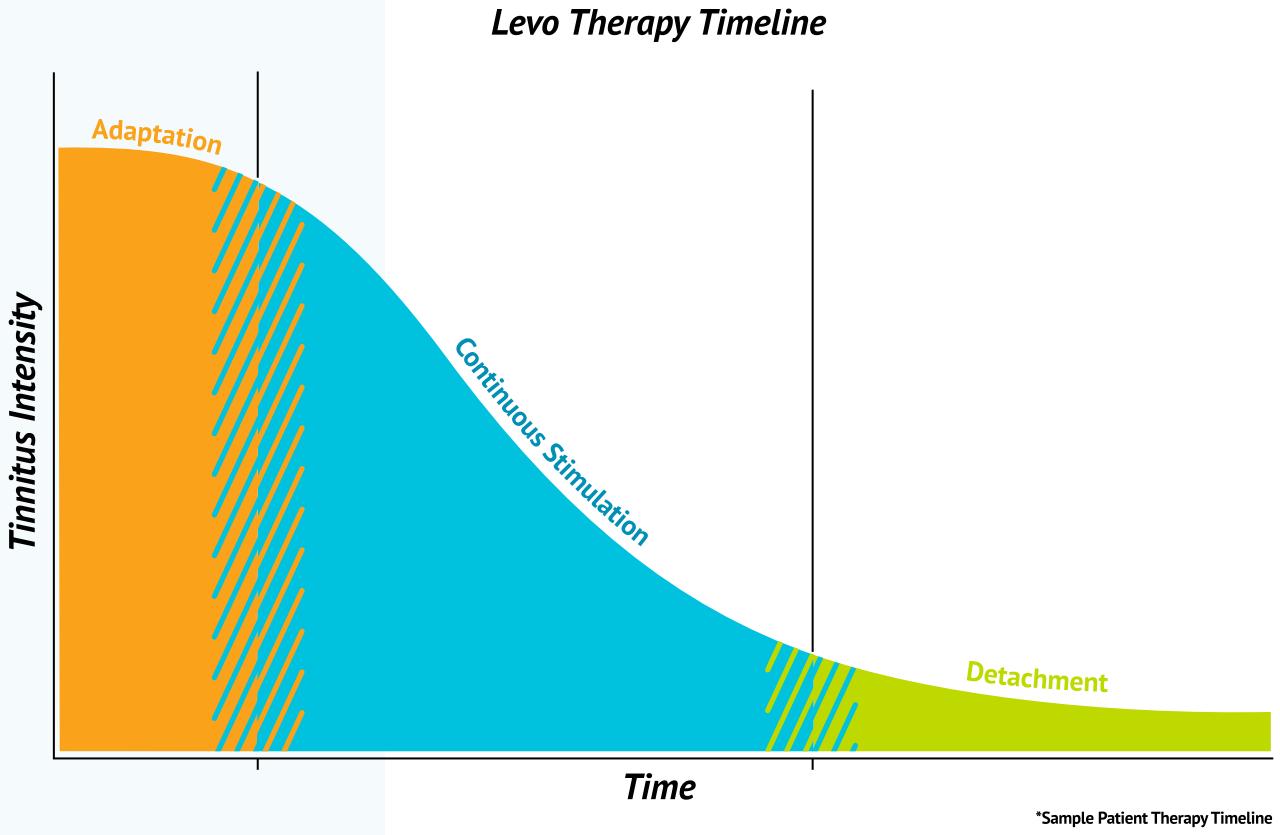

Figure 1

9 months evolution
(60 patients)

Figure 2

Levo Outcomes

Published data from a preliminary prototype of the Levo system showed a significant decrease in perceived tinnitus loudness with some patients even reporting periods of total silence during a period of 6 months (Pedemonte, 2010).

Clinical evidence from another study performed using the Levo system showed sound intensity level reduction of 14.1 dB on average (Drexler, 2016) which correlates to a reduction of 80% of the original sound intensity. Since a reduction of 10 dB in sound intensity levels decreases the loudness perception by half, the perceived tinnitus loudness displayed an average reduction of 62% compared to pre-treatment values. This reduction was directly correlated to an overall improvement in the patients' quality of life. A reduction in the Tinnitus Handicap Inventory, Tinnitus Reaction Questionnaire and Tinnitus Functional Index (TFI) scores of 62%, 65% and 78% respectively was measured. The mean decrease observed for TFI was 48 points, with statistically significant decrease for the intrusive, sense of control, emotional, and quality of life subscales. Especially relevant improvements were observed for sleep and relaxation subscales, which had reductions of 55.1 and 52.7 points, respectively.

The Levo System was used in another independent study at the National Center for Rehabilitative Auditory Research (NCRAR) at VA Portland Health Care System, which showed on the numeric rating scale for tinnitus with at least 95% certainty, a greater reduction in tinnitus loudness than non-customized sound treatment with bed side sound generator also applied during sleep. This study also showed that a new subject would have a 74% chance of improvement on the numeric rating scale of tinnitus and a 91% in quality-of-life measures with the Levo therapy (Theodoroff, 2017).

A recent meta-analysis performed on data from 60 subjects with tinnitus, as summarized in figure 2, treated with the Levo System at the 'Centro de Tinnitus Montevideo' in Uruguay between 2015 and 2022, showed that on patients that made a 9 month consistent treatment, 25.61% achieved more than 10dB of sound level reduction (corresponding to half the tinnitus loudness), 32.07% between 5dB and 10dB of reduction and 27.29% less than 5dB of reduction (a perceivable decrement on tinnitus loudness). Overall, 84.96% of patients achieved some degree of tinnitus intensity level reduction.

Conclusion

The Levo System proved to be an effective therapy to reduce both the loudness of the tinnitus and the negative impacts on a patient's quality of life. The Levo system also proved to be better at improving quality-of-life than non-customized sound stimulation such as bedtime noise generators.

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The Levo System is an FDA-cleared medical device that provides patients a patented personal sound therapy which through neural habituation leverages the cognitive abilities of the brain to reduce the symptoms of their tinnitus and improve the quality of a patient's daily life.

Learn more at levomedical.com