

Tinnitracks

Information on effectiveness



Innovations- und
Entrepreneurpreis 2013
Gesellschaft für Informatik

GRÜNDERWETTBEWERB
IKT INNOVATIV



IFB
HAMBURG | Hamburgische
Investitions- und
Förderbank

HEIDELBERGER
INNOVATIONEN FORUM

Deutschland
Land der Ideen
© 2013

9th edition
Sonormed GmbH, Hamburg 2015

Contents

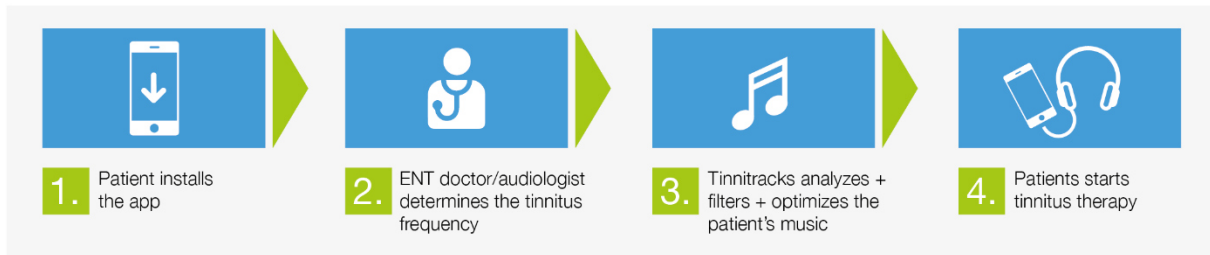
1. Overview	1
2. Tinnitracks – Correct application of the TMNMT procedure.....	3
3. Neuroscientific and medical principles of TMNMT	5
3.1 Experimental findings from neuroscientific studies.....	6
3.2 Experimental findings from clinical studies	10
4. Tips for practical use	15
4.1 Inclusion criteria: Which patients can benefit from Tinnitracks?.....	15
4.2 User information: How should Tinnitracks be used?.....	15
References.....	16

1. Overview

Tinnitracks is an app for smart phones and computers that enables tinnitus patients to use their favorite music to create a reliable, tailored tinnitus therapy that is neuroscientifically valid.

This CE-certified medical product systematically implements the relevant findings of modern brain science and was developed based on tailor-made notched music training (TMNMT).

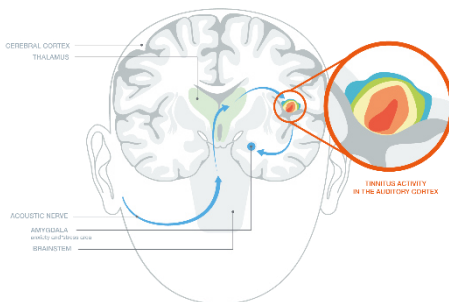
With its engineering innovations, Tinnitracks is the first to provide patients with a simple and reliable app for individual tinnitus therapy suitable for everyday use.



➔ See 2. Tinnitracks – Correct application of the TMNMT procedure

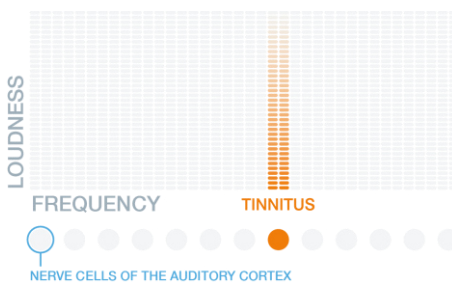
page 3

In recent years, modern brain research, in both clinical studies and basic research, has produced a number of decisive new findings on tinnitus:



Subjective tonal tinnitus is associated with a flawed organization within the auditory cortex and with an increased excitability of the nerve cells within the auditory cortex.

The primary triggers for the development of tinnitus are thought to be deafferentation of central auditory structures and the sensory deprivation that this causes in downstream stations in auditory processing. Reduced sensory input leads to changes in neural connectivity.



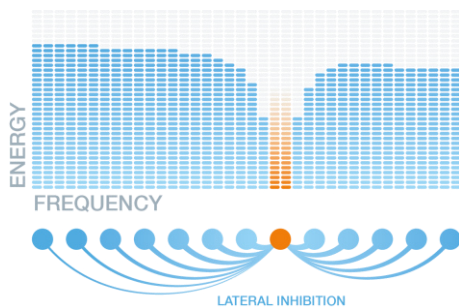
These changes can result in mismatched reorganization of neural connections, from which an imbalance of excitatory and inhibitory nerve activity emerges. This leads to hyperactivity of nerve cells, which can manifest itself as tinnitus. This overexcitability can be localized to specific nerve groups in the auditory cortex, which correspond to the perceived tinnitus frequency.

For these reasons, tinnitus is currently considered a disorder that is based on misguided neural plasticity.

➔ See 3. Neuroscientific and medical principles of TMNMT

page 5

While previous therapy forms often only treat the symptoms, Tinnitracks enables the targeted treatment of the causes underlying tinnitus, using tailor-made notched music training with the help of the patient's favorite music.



For the therapy, the patient's selected music is filtered such that the signal components in the range of the individual tinnitus frequency are completely removed.

When the brain processes this frequency-filtered music, an inhibitory activity arises in the central structures of the brain, which counteracts the overexcitability of specific neuron groups in the auditory cortex associated with tinnitus.

It is known from basic neuroscience research that frequency-filtered audio signals can effect a specific attenuation in auditory processing. The neural mechanism underlying this reduction in auditory processing is lateral inhibition within the neural networks. Lateral inhibition is a type of connectivity that serves as a basic mechanism in several sensory systems and is important for local processing of sensory information.

Neurophysiological studies have shown that lateral inhibition in the auditory networks of the brain can be stimulated by listening to frequency-filtered, specifically processed audio signals.

➔ See 3.1 Experimental findings from neuroscientific studies page 6

Through repeated and regular use of the TMNMT procedure, the auditory networks establish an inhibitory influence on the tinnitus-associated hyperactivity in the cortex, thereby permanently counteracting the cause underlying tinnitus.

So Tinnitracks takes advantage of the principle of neural plasticity to reverse the effects of the inappropriate reorganization, and it does it by specifically altering the sensory environment: patients listen to their favorite music, which has been specifically filtered to accommodate their individual tinnitus frequencies.

The long-term effectiveness of the TMNMT procedure has been tested in several independent clinical studies and confirmed repeatedly on tinnitus patients. The therapy effects proved consistent on both behavioral and neurophysiological levels.

➔ See 3.2 Experimental findings from clinical studies page 10

The TMNMT procedure used by Tinnitracks is based on the published studies listed below, and with the approval of the treating physician, it can be used for all patients whose subjective chronic tinnitus exhibits a stable frequency.

➔ See 4. Tips for practical use page 15
4.1 Inclusion criteria: Which patients can benefit from Tinnitracks?
4.2 User information: How should Tinnitracks be used?

2. Tinnitracks – Correct application of the TMNMT procedure

Tinnitracks is Sonormed's technical solution for an easy-to-use tailor-made notched music training (TMNMT)-compliant music processing application. Thanks to multiple technical innovations, it is both reliable and automated.

Tinnitracks is a CE-certified medical device in the form of an app for smartphones and computers. It provides tinnitus patients and medical personnel with the first simple, safe tool for implementing TMNMT.

This evidence-based therapy can be easily integrated into daily life: it is portable and can be done while the patient is doing other things, and it doesn't require any medication. The therapy also provides an inherently high compliance, since listening to their favorite music is something many patients already do every day.

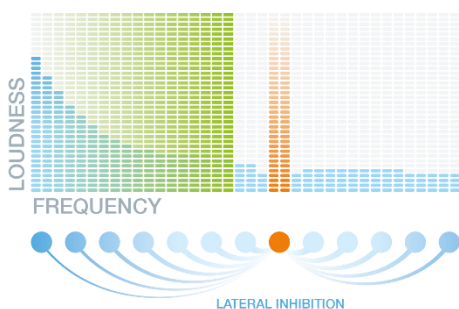
Automatic music processing – reliable, precise and convenient

All of Tinnitracks' technical processes have been reliably automated in order to eliminate user error and make it extremely easy to use. This enables patients to create their own therapy from their favorite music.

Individual analysis of the therapy potential of each piece of music

In addition to the individual filtering of the patient's selected music, Tinnitracks also offers additional functions that enable the patient to create a reliable tinnitus therapy from his or her own music.

Tinnitracks is the only solution offering (full) control of the therapeutic potential of the processed music. This is crucial because not every song title possesses the frequency spectrum that can activate the compensatory brain processes for the patient's individual tinnitus frequency.



Therapy potential analysis: an example of an inefficient song

That's why Tinnitracks uses a neuroacoustic model to test each song selected by the user and analyze whether the song is suitable for therapy.

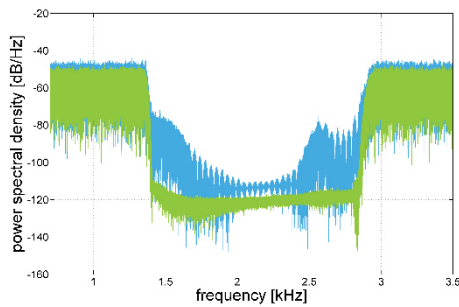
The result of the therapy potential analysis is revealed to the patient as a colored symbol: a red light indicates poor suitability; a green light indicates a highly suitable song. This enables the control over and, if necessary, the elimination of therapeutically inefficient music from the therapy plan. So the patient can use his or her own music for therapy, independently and reliably.

User assistant and quarterly statistics for correct therapy administration

By recording and analyzing the daily usage and presenting the data in a form that is easy to understand, Tinnitracks assists the patient in the correct administration of the therapy. This enables the patient to fully concentrate on listening to his or her filtered music, rather than spending time documenting the completed therapy units. The treating physician or audiologist has access to comprehensive quarterly statistics on the amount of time spent listening.

Therapeutically correct MP3 encoding

Tinnitracks is also the only app that can save the processed music files in the space-saving MP3 format and maintain the quality necessary for an effective therapy:



Filtered noise encoded with Tinnitracks' MP3 procedure (green), with conventional MP3 procedure (blue)

Every other available application for MP3 compression substantially reduces the therapeutic quality of the processed music; some even alter the music so much that it is unusable for tinnitus therapy. The compression procedure leads to an accumulation of quantization noise in the filtered frequency range.

Tinnitracks' MP3 encoding procedure was specially developed for the TMNMT procedure. It maintains the patient-specific therapeutic filtering, making Tinnitracks the only product that guarantees the therapeutic quality of processed music in the space-saving MP3 format.

Optimal integration of software und hardware

The frequency response of the headphones used for the therapy should be as linear as possible. That means that they should not amplify or mute any frequency ranges and should present a completely neutral sound pattern. However, in order to provide a pleasant sound, headphones are generally not linear or neutral over the entire frequency range.

That's why Tinnitracks, in collaboration with Sennheiser, offers an optional equalization of the therapy music for selected headphone models, which are also available with Tinnitracks as a package:

Tinnitracks amplifies or mutes those frequencies that the headphone model purchased with Tinnitracks dampens or enhances (for example, bass enhancement): the frequency response is precisely compensated. This enables the processed music to be played through the patient's headphones without enhancing any specific frequencies (linear frequency response).

The exceptional quality of Sennheiser headphones guarantees a consistently high build quality and a low component tolerance. This makes these headphones excellent for the frequency response equalization through Tinnitracks and for TMNMT therapy.

Internet-based data synchronization conserves batteries in mobile devices

Tinnitracks is an internet-based app, so patients can always use the most recent version. The patient benefits from immediate access to any updates, and the therapy is always administered with the most up-to-date research and technology.

The server-supported infrastructure also saves batteries: Playing the music processed for therapy does not require any more power than listening to normal music on a smart phone, since the filtering of the music with high-power filters, the therapy potential analysis of the selected music, and the head phone optimization are not performed by the smart phone, but by the Tinnitracks servers. That's how Tinnitracks achieves an excellent level of processing while conserving the patient's smart phone battery.

3. Neuroscientific and medical principles of TMNMT

While some processes involved in the development and persistence of tinnitus are not yet fully understood, modern brain science has made significant progress towards understanding the physiological principles of subjective tonal tinnitus.

Subjective tinnitus is a phantom perception: it is the perception of a sound (or tone) in the absence of an acoustic source. This type of perception is often thought to be related to the phantom perception that occurs when a limb is missing, and is frequently compared with phantom pain (Jastreboff, 1990; Ridder et al., 2011).

In the past few years, intensive clinical research and basic studies have brought about a series of decisive new results. Subjective tonal tinnitus was shown to be associated with a faulty organization within the auditory cortex and with an abnormally high excitability of the nerve cells in the auditory cortex. This hyperexcitability of specific neuron groups in the auditory cortex is considered to be the mechanism underlying the perception of tinnitus (Eggermont and Roberts, 2004, 2012; Kaltenbach, 2011; Stein et al., 2014).

The primary trigger for the development of tinnitus is thought to be the deafferentation of the central auditory structures through damage to the cochlea (the damage can be hidden and only discovered years after the injury) and the resulting sensory deprivation of the downstream stations in auditory processing. Because of the brain's plasticity, reduced sensory input leads to reorganization and thus to changes in neural connections (Møller, 2011). This reorganization can lead to mismatched neural connections, which can cause an imbalance in excitatory and inhibitory nerve cell activity; this leads to hyperactivity of nerve cells, which can manifest itself as tinnitus (Diesch et al., 2010a, 2010b; Eggermont and Roberts, 2004, 2012; Møller, 2011).

For this reason, current brain research considers tinnitus to be a disorder that is caused by misguided neural plasticity. Specifically, the misguided reorganization in the auditory cortex following a previous injury to the sensory periphery (the inner ear or cochlea) and the resulting increased excitability of the auditory neuron groups are decisive factors in the formation and maintenance of chronic subjective tinnitus (Herraiz et al., 2009).

The fact that the adult brain dynamically reacts to the external sensory environment and remains plastic has been known for many years. The neural building blocks of the brain, and thus the brain itself, is in no way a hard-wired, rigid structure, but is constantly changing and can adapt flexibly to the dynamic changes in the environment. The experience-based reorganization of the brain is called neuroplasticity. The sensory-driven reorganization can lead to both functional and structural changes in neurons and entire neural networks (Bear et al., 2008; Dudel et al., 2001; Reichert, 2000).

The emergence of neuroplasticity has been established in several sensory systems (for example visual, auditory, somatosensory), in motor connectivity patterns, and in general on the level of the cortex. It is considered an important principle for the dynamic arrangement of the neural architecture and function in the adult organism (Kandel et al., 2000).

The principle of neural plasticity can be used to reverse the results of misguided reorganization, namely by specifically designing the sensory environment by presenting filtered auditory signals. And this is the approach taken by the TMNMT procedure, which has been realized with Tinnitracks.

3.1 Experimental findings from neuroscientific studies

The following will present and describe those scientific findings and specific results from tinnitus research in connection with the tailor-made notched music training (TMNMT) that form the basis for the development of Tinnitracks.

Pantev, Roberts, Wollbrink, Engelien, Lütkenhöner (1999): Short-term plasticity of the human auditory cortex

This study examines the effect of frequency-filtered music on the subsequent processing of auditory information within the cortex.

To this end, healthy participants (n=10) listened for 3 hours on 3 successive days to their favorite music, from which a narrow frequency range (center frequency: 1 kHz) had been removed. Immediately after listening to this frequency-filtered music, the participants were presented with two different tones: a test tone, with a center frequency of 1 kHz, and a control tone of 0.5 kHz. The test tone corresponded to the frequency range that had been removed from the music that the participant had just heard. While the participants listened to these tones, their brain activity was recorded using magnetoencephalography (MEG). The neural activity that was triggered by each tone was analyzed and compared: the 1 kHz tone triggered a lower neural activity than did the 0.5 kHz control tone.

This result indicates that fast changes in the response behavior of nerve cells in the human cortex can be induced when the acoustic environment is manipulated in a frequency-specific manner. The authors suggest a dynamic form of neural plasticity as the mechanism underlying the observed effects.

Conclusions:

- The processing of auditory information in the brain can be influenced by the targeted manipulation of the sensory experience, that is, by listening to frequency-filtered music.
- Listening to frequency-filtered music leads to a stimulus-specific, selective reduction in cortical neural activity. This reduction is frequency specific: it only occurs during processing of the tone with the same center frequency as the music filter.
- The reduction in neural activity, triggered by frequency-reduced music, is a cumulative, transient, and reversible process.
- These changes in the response behavior of auditory neuron groups are thought to be based on a specialized form of connectivity that exerts inhibitory influence within the auditory system (lateral inhibition).

Source:

- Pantev, C., Wollbrink, A., Roberts, L.E., Engelien, A., and Lütkenhöner, B. (1999). Short-term plasticity of the human auditory cortex. *Brain Res.* 842, 192–199.

Pantev, Okamoto, Ross, Stoll, Ciurlia-Guy, Kakigi, Kubo (2004): Lateral inhibition and habituation of the human auditory cortex

This study examines the effects of different forms of noise on the subsequent processing of auditory information in the auditory cortex.

To this end, healthy subjects (n=10) listened to 3 seconds of noise, followed by a complex test signal (composed of 5 different frequency components), while their brain activity was recorded via magnetoencephalography (MEG). One variant of the noise signal was composed of a periodic spectrum with interjacent frequency gaps (the center frequencies of the notch filter were within a half octave of each other, from 0.5 kHz to 2.8 kHz). The test signal was composed either of frequency components found in exactly these gaps (SB stimuli) or of components with the same center frequencies as the noise (PB stimuli). Based on previous studies, frequency-reduced noise was expected to lead to a reduction in the subsequent auditory processing of both stimuli. Different neural mechanisms are thought to be responsible for the reduction in auditory processing of the two stimulus types. The stimuli with the frequency gaps in the noise signal (SB stimuli) should lead to a reduction in auditory processing as a result of lateral inhibition. The stimuli whose frequency components are identical to the noise signal (PB stimuli) should trigger a reduction in cortical processing as a result of response reduction following repetitive stimulation. In addition to frequency-reduced noise, the effects of broadband white noise were examined.

This study showed that both habituation and lateral inhibition can cause a reduction in auditory cortex activity. The effect of lateral inhibition was approximately 14% stronger than the reduction caused by habituation. White noise also caused a reduction in auditory processing for both stimuli, but the effect was smaller than for the other two conditions and did not differ between the two stimulus conditions.

Conclusions:

- The processing of auditory information in the brain can be reduced by noise presented immediately before the stimulus.
- A noise signal causes the largest reduction in cortical processing when the auditory signal is composed of frequency components found in the gaps of the frequency-reduced noise signal.
- In comparison to frequency-filtered noise, white (not frequency-reduced) noise leads to a small reduction in neural processing of auditory stimuli.

Source:

- Pantev, C., Okamoto, H., Ross, B., Stoll, W., Ciurlia-Guy, E., Kakigi, R., and Kubo, T. (2004). Lateral inhibition and habituation of the human auditory cortex. *Eur. J. Neurosci.* 19, 2337–2344.

Okamoto, Kakigi, Gunji, Pantev (2007): Asymmetric lateral inhibitory neural activity in the auditory system: a magnetoencephalographic study

The reduction of auditory-evoked brain signals through repeated presentation of similar tones—that is, tones with similar frequency properties—is a well-documented and frequently replicated finding from electro- and magnetoencephalography (EEG/MEG). The study described here aimed to examine more closely the possible role of inhibitory interaction between different neuron groups during this reduction.

Specifically, MEG was used to examine what effect frequency-filtered noise has on the subsequent neuronal processing of test tones. The frequency content of the filtered noise was changed specifically in the experiment. Five different variants of frequency-filtered noise were presented to the participants (n=9) for 3 seconds before they heard a 1 kHz test tone, while their brain activity was recorded by MEG. Using a notch filter with a bandwidth of an octave, each of the noise variants was changed such that the lower spectral border frequency was a different distance from the 1 kHz test tone. This enabled the noise to stimulate different neuron groups with different receptive fields.

The analysis showed that brain activity triggered by the test tone (N1m component) was reduced by different amounts by the previously presented noise. The noise variant with a lower spectral border frequency closest to the test tone caused the strongest reduction in auditory processing. The authors interpret this reduction as a manifestation of lateral inhibition, whereby the extent of the inhibitory interaction of neighboring neuron groups with different receptive fields depended on the frequency content of the previously presented noise signal.

Conclusions:

- The processing of auditory information in the brain, represented by the N1m component, is reduced to a differing extent depending on the frequency components of the noise.
- The frequency-filtered noise signal with a lower spectral border frequency closest to the test tone caused the strongest reduction in auditory cortical activity.
- The reduction in cortical activity caused by noise is thought to be a result of the inhibitory influence of neighboring neuron groups with different receptive fields (lateral inhibition).

Source:

- Okamoto, H., Kakigi, R., Gunji, A., and Pantev, C. (2007). Asymmetric lateral inhibitory neural activity in the auditory system: a magnetoencephalographic study. *BMC Neurosci.* 8, 33.

Stein, Engell, Okamoto, Wollbrink, Lau, Wunderlich, Rudack, Pantev (2013): Modulatory Effects of Spectral Energy Contrasts on Lateral Inhibition in the Human Auditory Cortex: An MEG Study

Several studies have shown that frequency-filtered noise leads to a reduction in the subsequent auditory processing, which is reflected in a reduction in the N1m component. The neural mechanism underlying this reduction is thought to be lateral inhibition within the auditory networks. This type of connectivity is a fundamental mechanism in other sensory systems as well, and underlies local processing of sensory information. Neurophysiological studies indicate that the influence of lateral inhibition on the processing power of auditory stimuli can be controlled by applying notch filters of given bandwidths.

The study outlined here investigates which additional filter parameters can alter the noise such that the reduction in the subsequent auditory processing is maximized. To this end, various technical parameters were systematically manipulated; for example, the signal components were reduced or amplified by 30 dB within the range of the upper and lower border frequencies of the filter. The bandwidth of the amplification of the filter's upper and lower border frequencies was also altered (3/8 or 7/8 octave). The different variants of frequency-filtered noise were presented to participants (n=16 and n=11) for 3 seconds before they heard a 1 kHz test tone; the participants' brain activity was recorded using magnetoencephalography (MEG).

The analysis of the neuronal activity within the auditory cortex triggered by the test tone showed that the reduction in the N1m component was modulated by the previously presented noise. The strongest reduction in neural activity was achieved with the amplification of the signal components on the filter's border frequencies, whereby the bandwidth of the amplification was kept as narrow as possible. These results indicated that by optimizing the filter properties, neuron groups with specific receptive fields can be increasingly activated, thereby enhancing the influence of lateral inhibition within the auditory networks.

Conclusions:

- The reduction in processing of auditory information in the brain can be increased by altering the filter parameters of frequency-filtered noise presented immediately previous to the stimulus.
- The enhancement of the signal components in the border frequencies of the filter (and thus a contrast enhancement of the edge region, between the band that permitted signal passage and the band that did not) achieved the strongest reduction in auditory activity in the cortex.
- The pattern of the reduction in auditory activity through the filter properties indicates the influence of lateral inhibition within the auditory networks.

Source:

- Stein, A., Engell, A., Okamoto, H., Wollbrink, A., Lau, P., Wunderlich, R., Rudack, C., Pantev, C. (2013). Modulatory effects of spectral energy contrasts on lateral inhibition in the human auditory cortex: an MEG study. PLoS One, 8(12): e80899.

3.2 Experimental findings from clinical studies

Okamoto, Stracke, Stoll, Pantev (2010): Listening to tailor-made notched music reduces tinnitus loudness and tinnitus-related auditory cortex activity

Stracke, Okamoto, Pantev (2010): Customized notched music training reduces tinnitus loudness

As mentioned above, current research regards tinnitus as a disorder that arises from misguided neural plasticity. The reorganization of the cortex is recognized as the decisive factor in the development and maintenance of subjective tinnitus.

Because cortical reorganization can be altered by behavioral training, this study aimed at reducing the tinnitus loudness in chronic tinnitus patients by having them listen to pleasant music that they selected themselves and was specifically processed for their individual tinnitus frequencies. The music used for the training was frequency filtered using a notch filter in the individual tinnitus frequency. This filtering removes the signal components within the individual tinnitus frequency range (TMNMT method).

The tinnitus patients listened to the music regularly over a period of 12 months (1-2 hours per day). The brain activity of the patients was measured using magnetoencephalography (MEG) before the start of the music training, half way through the training period, and after the training period. In order to assess the neural activity of the cortex during the processing of auditory stimuli, the patients were presented with repeated tones at 500 Hz and in their individual tinnitus frequencies.

After completion of the music training, patients in the therapy group reported a reduction in subjective tinnitus loudness and showed a reduction in auditory cortex activity during the processing of stimuli in the individual tinnitus frequency. In the placebo group, in which the tinnitus patients listened to music that was filtered at a frequency that was not the tinnitus frequency, no change was observed: neither the subjective tinnitus loudness nor the neural activity in the auditory areas changed over the study period. In the control group, in which tinnitus patients did not participate in music training, there were also no measurable effects.

These results show that subjective tinnitus loudness can actually be reduced by listening to pleasant music that has been individually filtered. The observed effects indicate a reversal of the misguided reorganization of the auditory cortex.

Conclusions:

- This longitudinal double-blind study was carried out on chronic tinnitus patients (n=39) who were pseudo-randomly divided into three groups: therapy group, placebo group, and control group.
- Listening to music filtered with the individual tinnitus frequency (tailor-made notched music training, TMNMT) led to a decrease in tinnitus loudness and to a reduction in neural activity in the auditory cortex. Both effects were visible in the therapy group after the first 6 months of music training and differed significantly from the starting values.
- The reduction in tinnitus loudness reported by the therapy group correlated with the reduction in neural activity in the primary auditory cortex (auditory steady state response, ASSR).
- Characteristics of the tinnitus patients: the patients (age range: 18 – 55 years) suffered from a tonal, strongly lateralized tinnitus with a frequency ≤ 8 kHz. The patients did not exhibit a strong hearing loss (less than 35 dB HL) and were free of neurological and psychiatric complications.

Sources: See next page

Sources:

- Okamoto, H., Stracke, H., Stoll, W., and Pantev, C. (2010). Listening to tailor-made notched music reduces tinnitus loudness and tinnitus-related auditory cortex activity. *Proc Natl Acad Sci USA* *107*, 1207–1210.
- Stracke, H., Okamoto, H., and Pantev, C. (2010). Customized notched music training reduces tinnitus loudness. *Commun Integr Biol* *3*, 274–277.

Lugli, Romani, Ponzi, Bacciu, Parmigiani (2009): The windowed sound therapy: a new empirical approach for an effective personalized treatment of tinnitus

In this study, an auditory stimulation therapy was carried out on patients with chronic, tonal subjective tinnitus ($n = 43$), with the aim of achieving a long-term reduction in perceived tinnitus loudness.

The effect of frequency-filtered noise, specifically filtered in the individual tinnitus frequency of the respective patient, was ascertained by regularly recording the changes in perceived tinnitus loudness over a time period of 2 to 12 months. Those patients who were randomly assigned to one of the two control groups listened to either unfiltered broadband noise or the unfiltered noise of a waterfall for 1½ to 3 hours per day for the 1-year training phase.

Those patients that listened to frequency-filtered noise showed a long-term, consistent reduction in perceived tinnitus loudness. This effect was not observed in patients in the two control groups.

The important conclusion that the authors emphasize is that a personalized, individual application is decisive for the development of an effective tinnitus therapy based on auditory stimulation.

Conclusions:

- Listening to frequency-reduced noise that is specifically filtered in the individual tinnitus frequency leads to a long-term reduction in perceived tinnitus loudness.
- Unfiltered broadband noise, on the other hand, had no measureable effect on the participating tinnitus patients.
- Characteristics of the tinnitus patients: the patients suffered from chronic (≥ 5 months) subjective tonal tinnitus with a frequency between 1 and 13 kHz. The patients exhibited a hearing loss with maximal values between 10 and 100 dB HL.

Source:

- Lugli, M., Romani, R., Ponzi, S., Bacciu, S., and Parmigiani, S. (2009). The windowed sound therapy: a new empirical approach for an effective personalized treatment of tinnitus. *Int. Tinnitus J.* *15*, 51–61.

Teismann, Okamoto, Pantev (2011): Short and Intense Tailor-Made Notched Music Training against Tinnitus: The Tinnitus Frequency Matters

This study examined the effects of frequency-filtered music (TMNMT) on tinnitus patients ($n = 24$) when applied in the form of a short (5 consecutive days) and intensive (up to 6 hours per day) training. Specifically, the effect of TMNMT on individual tinnitus perception (tinnitus loudness and tinnitus-related distress) and on the level of neural activity in the cortex was examined. In addition, the persistence of the TMNMT treatment effect was observed over a time period of 4 weeks following the training.

Participants in this study were patients with chronic, tonal tinnitus who were divided into two groups depending on their perceived tinnitus pitch: patients with low (≤ 8 kHz) and high tinnitus frequencies (> 8 kHz). Before treatment and several times following treatment (3 hours afterwards and 3, 17 and 31 days later), the patients were examined. While their brain activity was being measured with magnetoencephalography (MEG), the patients were presented with control tones at 500 Hz and tones in their individual tinnitus frequencies, and their momentary tinnitus perception was determined.

The results showed that for patients with low tinnitus frequencies (≤ 8 kHz), short, intensive music training led to a reduction in tinnitus loudness and perceived tinnitus-related distress. These patients also exhibited a reduction in auditory processing of stimuli within the tinnitus frequency, in higher-level auditory areas in the cortex that all responded in the first 100 ms after stimulus presentation (N1m response). These effects fluctuated over the observation period of several weeks, both on the perceptual level and on the neural level. Music training had no measureable effect on patients with high tinnitus frequencies (> 8 kHz).

Conclusions:

- For patients with low tinnitus frequencies (≤ 8 kHz), short and intensive music training with frequency-filtered music was able to reduce the perceived tinnitus loudness and tinnitus-related distress, as well as the neural processing of tones in the respective tinnitus frequency.
- Both the onset as well as the duration of the effects on the level of perception (tinnitus loudness and distress) and brain activity followed complex patterns. Over the 4-week observation period after the completion of the music training, the reduction in tinnitus-related distress increased with time, while the reduction in tinnitus loudness was observed as early as 3 hours post-training. The effect on tinnitus loudness disappeared 3 days later and was observed once more at the middle of the observation period.
- Filter properties: the online filtering process consisted of two steps. In the first step, the frequency spectrum of the music was flattened over all frequencies. Second, a frequency range with a bandwidth of 1 octave, centered on the tinnitus frequency, was removed from the music.
- Patient characteristics: the patients suffered chronically (≥ 3 months) from tonal tinnitus; they were divided into two groups depending on whether their tinnitus frequency was ≤ 8 or > 8 kHz. The patients exhibited no hearing losses greater than 50 dB HL for the frequency range between 125 and 16000 Hz.

Source:

Teismann, H., Okamoto, H., & Pantev, C. (2011). Short and intense tailor-made notched music training against tinnitus: the tinnitus frequency matters. *PLoS one*, 6(9), e24685.

Stein, Engell, Junghoefer, Wunderlich, Lau, Wollbrink, Rudack, Pantev (2014): Inhibition-induced plasticity in tinnitus patients after repetitive exposure to tailor made notched music

Several studies have reported that frequency-filtered music can elicit frequency-specific inhibition within auditory processing. The study outlined here examines in detail which cortical structures are influenced by frequency-filtered music (tailor-made notched music training, TMNMT) in tinnitus patients and how this inhibition-induced plasticity develops temporally in the brain.

To this end, patients (n = 9) with chronic, tonal tinnitus listened to frequency-filtered music for 3 hours on three consecutive days. This music was frequency-specifically reduced by filtering it on a notch filter on the individual tinnitus frequency (TMNMT method). Before and after listening to the music, the patient was presented with a control tone at 500 Hz and a tone at his or her individual tinnitus frequency. While listening to these tones, the patient's brain activity was recorded using magnetoencephalography (MEG). In addition, the subjective perception of the tinnitus loudness was assessed using a visual analog scale.

Listening to frequency-filtered music led to a reduction in the subjective perception of tinnitus loudness and a reduction in processing of the auditory stimuli in the temporal, parietal and frontal areas of the cortex, all of which responded within the first 100 ms after the stimulus presentation (N1m response). The reduction in activity in the temporal and frontal areas was significantly correlated with the reduction in perceived tinnitus loudness. The reduction in neural activity corresponding to the processing of tones with the respective tinnitus frequencies persisted throughout the observation period and increased cumulatively over these three days.

Conclusions:

- In patients with chronic, tonal tinnitus, a three-day, short-term TMNMT led to a reduction in perceived tinnitus loudness and a decrease in neural processing of tones with the respective tinnitus frequency.
- This reduction in neural activity was not limited to auditory areas (temporal region), but included an entire network of areas within the parietal and frontal cortex.
- The subjective perception of tinnitus loudness decreased to the same extent as the neural activity in the temporal and frontal areas (significant correlation between subjective perception and brain activity).
- Filter properties: the online filter was modified in two aspects. Firstly, the frequency spectrum was flattened over all frequencies according to Teismann et al. (2011). Next, a frequency range with a bandwidth of $\frac{1}{2}$ octave, centered over the tinnitus frequency, was removed from the music.
- Characteristics of the patient group: the patients suffered chronically (> 3 months) from a tonal tinnitus with a frequency between 1.8 and 8.5 kHz. The patients exhibited no hearing loss larger than 65 dB HL for the frequency range $\frac{1}{2}$ octave below to $\frac{1}{2}$ octave above the individual tinnitus frequency.

Source:

- Stein, A., Engell, A., Junghoefer, M., Wunderlich, R., Lau, P., Wollbrink, A., Rudack, C., and Pantev, C. (2014). Inhibition-induced plasticity in tinnitus patients after repetitive exposure to tailor-made notched music. Clin. Neurophysiol. Off. J. Int. Fed. Clin. Neurophysiol.

Pape, Paraskevopoulos, Bruchmann, Wollbrink, Rudack, Pantev (2014): Playing and listening to tailor-made notched music: Cortical plasticity induced by unimodal and multimodal training in tinnitus patients

As mentioned above, current research regards tinnitus as a disorder that arises from misguided neural plasticity. The reorganization of the cortex is recognized as the decisive factor in the development and persistence of subjective tinnitus. Listening to frequency-filtered music (music with no energy content in the specific individual frequency range of the tinnitus) can lead to inhibition of the respective neural activity in the auditory cortex (tailor-made notched music training, TMNMT).

Active production of music is known to be a strong trigger for brain plasticity, which can initiate changes in multiple sensory systems. The aim of this study was therefore to compare the effects of cortical plasticity in tinnitus patients (non-musicians) triggered either by attentive listening to frequency-filtered music or by actively learning to create frequency-filtered music. The authors hypothesized that listening (unimodal condition) and playing music (multimodal condition) would trigger different patterns of neural plasticity.

For this study, various behavioral parameters were ascertained for the patients ($n = 26/19$) and their brain activity was recorded using magnetoencephalography (MEG). The training lasted 2 months with daily sessions of 1 hour.

The results showed that only active listening to frequency-reduced music led to an actual change in the processing of tinnitus tones in the cortex, while active playing of filtered music did not cause any changes. The changes caused by the unimodal condition consisted of a reduction in activity in the temporal cortex and an increase in activity in the posterior parietal cortex.

Conclusions:

- Attentive listening to frequency-reduced music (tailor-made notched music training, TMNMT) led to neuroplastic changes in the reorganization of cortical networks in tinnitus patients.
- Active production of music had no measureable neuroplastic effects in auditory processing.
- Characteristics of the patient groups: the patients suffered chronically (≥ 3 months) from a tonal tinnitus with a frequency below 8.5 kHz. The patients had no hearing loss larger than 55 dB HL in the frequency range from 0.125 to 8.5 kHz.

Source:

- Pape, J., Paraskevopoulos, E., Bruchmann, M., Wollbrink, A., Rudack, C., and Pantev, C. (2014). Playing and Listening to Tailor-Made Notched Music: Cortical Plasticity Induced by Unimodal and Multimodal Training in Tinnitus Patients. *Neural Plast.* 2014, e516163.

4. Tips for practical use

4.1 Inclusion criteria: Which patients can benefit from Tinnitracks?

Based on the published literature listed here, and as long as the treating physician does not order otherwise, the tailor-made notched music training (TMNMT) implemented by Tinnitracks can be administered to patients with the following tinnitus criteria:

- Subjective, chronic tinnitus which has been present for more than 3 months
- Stable-tone tinnitus perception (with no fluctuation in the pitch). The phantom noise is narrow-band enough that a tinnitus frequency can be determined.
- Dominant tinnitus frequency under 8500 Hz
- No strong hearing loss (less than 65 dB HL)
- Age between 18 and 65 years

In addition, the treating physician has to rule out any further acute or chronic otological, neurological and psychiatric disorders, as well as alcohol and drug abuse.

4.2 User information: How should Tinnitracks be used?

The TMNMT application implemented by Tinnitracks should only be administered in consultation with the treating ENT doctor. Provided that the treating physician does not prescribe otherwise, the following directions apply:

- The patient should listen to his or her filtered music for at least 4 months for at least 90 minutes per day.
- The patient should listen to the music with headphones at a volume that is individually determined and that he or she perceives as pleasant.
- If a therapy session is briefly interrupted, the patient can continue and complete the session later.
- If a therapy session must be skipped, the patient can continue as usual with the next session on the following day.
- In some cases, directly following the treatment, the tinnitus can be perceived as louder when the surroundings become suddenly quiet (a contrast effect). This perception generally recedes after a few minutes.
- Tinnitus perception can change over time, sometimes appearing louder or quieter than other times. These perceptual fluctuations can also appear during treatment with filtered music. The long-term effects of the therapy are not affected by this phenomenon.
- Should the patient have the impression that the tinnitus is consistently louder, he or she should contact the treating physician.

References

- Bear, M.F., Connors, B.W., and Paradiso, M.A. (2008). *Neurowissenschaften - Ein grundlegendes Lehrbuch für Biologie, Medizin und Psychologie* (Berlin: Spektrum Akademischer Verlag).
- Diesch, E., Andermann, M., Flor, H., and Rupp, A. (2010a). Functional and structural aspects of tinnitus-related enhancement and suppression of auditory cortex activity. *NeuroImage* *50*, 1545–1559.
- Diesch, E., Andermann, M., Flor, H., and Rupp, A. (2010b). Interaction among the components of multiple auditory steady-state responses: enhancement in tinnitus patients, inhibition in controls. *Neuroscience* *167*, 540–553.
- Dudel, J., Menzel, R., and Schmidt, R.F. (2001). *Neurowissenschaft: Vom Molekül zur Kognition* (Berlin: Springer).
- Eggermont, J.J., and Roberts, L.E. (2004). The neuroscience of tinnitus. *Trends Neurosci.* *27*, 676–682.
- Eggermont, J.J., and Roberts, L.E. (2012). The neuroscience of tinnitus: understanding abnormal and normal auditory perception. *Front. Syst. Neurosci.* *6*.
- Goebel, G., & Hiller, W. (1994). The tinnitus questionnaire. A standard instrument for grading the degree of tinnitus. Results of a multicenter study with the tinnitus questionnaire. *HNO*, *42*(3), 166–172. <http://www.ncbi.nlm.nih.gov/pubmed/8175381>
- Herraiz, C., Diges, I., Cobo, P., and Aparicio, J.M. (2009). Cortical reorganisation and tinnitus: principles of auditory discrimination training for tinnitus management. *Eur. Arch. Oto-Rhino-Laryngol. Off. J. Eur. Fed. Oto-Rhino-Laryngol. Soc. EUFOS Affil. Ger. Soc. Oto-Rhino-Laryngol. - Head Neck Surg.* *266*, 9–16.
- Jastreboff, P.J. (1990). Phantom auditory perception (tinnitus): mechanisms of generation and perception. *Neurosci. Res.* *8*, 221–254.
- Kaltenbach, J. (2011). The Neuroscientist. In A. Möller, B. Langguth, D. de Ridder, & T. Kleinjung (Eds.), *Textbook of Tinnitus* (pp. 259–265). New York: Springer. <http://dx.doi.org/10.1007/978-1-60761-145-5>
- Kandel, E., Schwartz, J., and Jessell, T. (2000). *Principles of Neural Science, Fourth Edition* (McGraw-Hill Companies, Incorporated).
- Kreuzer, P. M., Vielsmeier, V., & Langguth, B. (2013). Chronic tinnitus: an interdisciplinary challenge. *Deutsches Ärzteblatt international*, *110*(16), 278–84. <http://dx.doi.org/10.3238/arztebl.2013.0278>
- Lanting, C. P., de Kleine, E., & van Dijk, P. (2009). Neural activity underlying tinnitus generation: results from PET and fMRI. *Hearing research*, *255*(1–2), 1–13. <http://www.ncbi.nlm.nih.gov/pubmed/19545617>
- Lugli, M., Romani, R., Ponzi, S., Bacciu, S., & Parmigiani, S. (2009). The windowed sound therapy: a new empirical approach for an effective personalized treatment of tinnitus. *The international tinnitus journal*, *15*(1), 51–61. <http://www.ncbi.nlm.nih.gov/pubmed/19842347>
- Meikle, M., & Taylor-Walsh, E. (1984). Characteristics of tinnitus and related observations in over 1800 tinnitus clinic patients. *The Journal Of Laryngology And Otology Supplement*, *9*, 17–21. <http://www.ncbi.nlm.nih.gov/pubmed/6596358>

- Menon, V., & Levitin, D. J. (2005). The rewards of music listening: response and physiological connectivity of the mesolimbic system. *NeuroImage*, 28, 175–84.
<http://www.ncbi.nlm.nih.gov/pubmed/16023376>
- Møller, A. (2011). The Role of Neural Plasticity in Tinnitus. In A. Møller, B. Langguth, D. de Ridder, & T. Kleinjung (Eds.), *Textbook of Tinnitus* (pp. 99–102). New York: Springer.
<http://dx.doi.org/10.1007/978-1-60761-145-5>
- Mühlnickel, W., Elbert, T., Taub, E., & Flor, H. (1998). Reorganization of auditory cortex in tinnitus. *Proceedings of the National Academy of Sciences of the United States of America*, 95(17), 10340–3. <http://www.pnas.org/content/95/17/10340.full>
- Okamoto, H., Kakigi, R., Gunji, A., and Pantev, C. (2007). Asymmetric lateral inhibitory neural activity in the auditory system: a magnetoencephalographic study. *BMC Neurosci.* 8, 33.
- Okamoto, H., Stracke, H., Stoll, W., & Pantev, C. (2010). Listening to tailor-made notched music reduces tinnitus loudness and tinnitus-related auditory cortex activity. *Proceedings of the National Academy of Sciences of the United States of America*, 107(3), 1207–1210.
<http://dx.doi.org/10.1073/pnas.0911268107>
- Pantev, C., Wollbrink, A., Roberts, L.E., Engelien, A., and Lütkenhöner, B. (1999). Short-term plasticity of the human auditory cortex. *Brain Res.* 842, 192–199.
- Pantev, C., Okamoto, H., Ross, B., Stoll, W., Ciurlia-Guy, E., Kakigi, R., and Kubo, T. (2004). Lateral inhibition and habituation of the human auditory cortex. *Eur. J. Neurosci.* 19, 2337–2344.
- Pantev, C., Okamoto, H., & Teismann, H. (2012a). Music-induced cortical plasticity and lateral inhibition in the human auditory cortex as foundations for tonal tinnitus treatment. *Frontiers in systems neuroscience*, 6(June), 50. <http://www.ncbi.nlm.nih.gov/pubmed/22754508>
- Pantev, C., Okamoto, H., & Teismann, H. (2012b). Tinnitus: the dark side of the auditory cortex plasticity. *Annals of the New York Academy of Sciences*, 1252(1), 253–8.
<http://www.ncbi.nlm.nih.gov/pubmed/22524367>
- Pape, J., Paraskevopoulos, E., Bruchmann, M., Wollbrink, A., Rudack, C., & Pantev, C. (in press). Playing and listening to tailor-made notched music: Cortical plasticity induced by unimodal and multimodal training in tinnitus patients. *Neural Plasticity*.
<http://www.hindawi.com/journals/np/aip/516163>
- Reichert, H. (2000). *Neurobiologie* (Stuttgart: Thieme).
- Ridder, D.D., Elgoyhen, A.B., Romo, R., and Langguth, B. (2011). Phantom percepts: Tinnitus and pain as persisting aversive memory networks. *Proc. Natl. Acad. Sci.* 108, 8075–8080.
- Stracke, H., Okamoto, H., & Pantev, C. (2010). Customized notched music training reduces tinnitus loudness. *Communicative integrative biology*, 3(3), 274–277.
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2918775/>
- Teismann, H., Okamoto, H., & Pantev, C. (2011). Short and intense tailor-made notched music training against tinnitus: the tinnitus frequency matters. *PloS one*, 6(9), e24685.
<http://dx.doi.org/10.1371/journal.pone.0024685>
- Weisz, N., & Langguth, B. (2010). Kortikale Plastizität und Veränderungen bei Tinnitus. *HNO*, 58, 983–989.
- Weisz, N. (2013). Aktuelle Trends aus der neurowissenschaftlichen Tinnitus-Forschung und deren klinische Implikationen. *Tinnitus-Forum*, 17(1), 18–21.

Wilson, E., Schlaug, G., & Pantev, C. (2010). Listening to filtered music as a treatment option for tinnitus: A review. *Music perception*, 27(4), 327–330.

<http://www.ncbi.nlm.nih.gov/pubmed/21170296>

Stein, A., Engell, A., Junghoefer, M., Wunderlich, R., Lau, P., Wollbrink, A., Rudack, C., Pantev, C. (2014). Inhibition-induced plasticity in tinnitus patients after repetitive exposure to tailor-made notched music. *Clinical Neurophysiology*, S1388-2457(14)00473-8.

<http://www.ncbi.nlm.nih.gov/pubmed/25441152>

Stein, A., Engell, A., Okamoto, H., Wollbrink, A., Lau, P., Wunderlich, R., Rudack, C., Pantev, C. (2013). Modulatory effects of spectral energy contrasts on lateral inhibition in the human auditory cortex: an MEG study. *PLoS One*, 8(12):e80899.

<http://www.ncbi.nlm.nih.gov/pubmed/24349019>

Contact

Do you have a question about Tinnitracks, or would you like to talk to us about another issue concerning Sonormed GmbH? The Tinnitracks Service Center is eager to hear your questions and suggestions.

Tinnitracks Service Center
Telephone +49 40 60945160
E-mail service@sonormed.de

Tinnitracks is provided by

Sonormed GmbH
Neuer Kamp 30
20357 Hamburg
Geschäftsführer: Jörg Land, Matthias Lanz
HRB 124315

www.tinnitracks.com



Innovations- und
Entrepreneurpreis 2013
Gesellschaft für Informatik

GRÜNDERWETTBEWERB
IKT INNOVATIV



IFB
HAMBURG | Hamburgische
Investitions- und
Förderbank

HEIDELBERGER
INNOVATION FORUM

Deutschland
Land der Ideen
Wettbewerb 2013