2013 Update: A Truly Critical Analysis of Tinnitus Theories and Therapies

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Questions
• How can multiple therapies with diametrically opposed methods all yield positive results?
  – Related to multiple loci of tinnitus, duration of tinnitus, patient personal factors
• Why haven’t we convinced medical world we can help tinnitus patients?
  – Lack of adequate sample size, independent studies, long term studies
  – So many successful therapies, yet Cochrane meta-analysis (Hobson, Chisholm, El-Rafaie, 2010) and recent Canadian review, lack of CPT codes and persistence of MDs saying “no cure”, “no help”, and “maskers” create doubt. Is there a way to change?
• What are realistic numbers with regard to success?
• Is there a “best” therapy?

Popular theories of tinnitus origin (apologies to those I’m omitting)
• Disruption of auditory input (e.g., hearing loss) and resultant increased gain (activity) within the central auditory system (including the dorsal cochlear nucleus and auditory cortex)
• Decrease in inhibitory (efferent) function
• Over-representation of edge-frequencies (cortical plasticity)
• Up-regulation of NMDA (N-methyl-D-aspartate) receptors increase aberrant excitation
• Other somatosensory influences (cervical disturbances, etc.)
• Association with fear and threat (limbic system)
• Increased attention related to reticular activating system involvement
• Dysfunctional gating in basal ganglia; thalamic reticul
Interpretation of Cheung and Larsen Results

- Instruction on details of phantom percepts are represented in the central auditory system.
- Permission to gate candidate phantom percepts for conscious awareness is controlled by the dorsal striatum.
- Action to attend, reject or accept phantom percepts, and form perceptual habits is decided by the ventral striatum.
- Determination of tinnitus distress severity is mediated through the limbic and paralimbic system-nucleus accumbens-ventral striatum loop.

Cheung and Larsen, Neuroscience 2010

Another “gatekeeping” theory

- The linked network of brain structures involved in emotion, behavior, and long-term memory—acts as a gatekeeper to keep the tinnitus signal from reaching the auditory cortex.
- Sensory information enters both the auditory and the limbic systems through the medial geniculate nucleus (MGN)
- Before the signal is processed, it travels through the thalamic reticular nucleus (TRN), which evaluates whether or not it should be passed on.
- There is a significant loss of volume in the medial prefrontal cortex (mPFC) in people with tinnitus. This structure projects into and activates the TRN. If the volume loss creates a loss of neurons, the mPFC and TRN will malfunction.

Rauschecker, et al; Neuron, 2010

Which one has a reduced medial prefrontal cortex?
Revised habituation model
(after Jastreboff and Hazell, 1993)

Perception & Evaluation
Auditory and Other Cortical Centers

Detection (Subcortical)

Emotional Associations — limbic system, frontal lobe cerebellum, etc.

Abnormal gating

Enabler

Annoyance

Dashed lines represent neutral interpretation of tinnitus percept.

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Tinnitus Therapies

- Reduce Contrast
- Mask Phantom Percept
- Suppress Hyperactivity

Examples:
- Maskers
- Hearing aids
- "Zen" Fractal tones
- Sound Cure S tones
- Cochlear implants

Tinnitus Therapies

- Reclassify Phantom Percept
- Reduce Saliency
- Mitigate Emotional Distress

Examples:
- Tinnitus Retraining Therapy
- Neuromonics
- Widex Zen Therapy
- Cognitive-behavioral therapy
- Mindfulness Based Stress Reduction
- Antidepressants
Tinnitus Therapies

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- Mask Phantom Percept
- Suppress Hyperactivity

Examples
- Hearing Aids
- "Neuromonics"
- "Zen" Fractal tones
- "Sound Cure" tones
- "Cochlear Implants"

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Examples
- Tinnitus Retraining Therapy
- Neuromonics
- "Zen" Therapy
- "Cochlear Implant" therapy
- "Sound Cure" therapy
- "Cochlear Implant" therapy

- Disrupt Information Conveyance
- Avoid Interference with Audition

Examples
- Striatal Neuromodulation
- Vagal nerve stimulation
- Cortical Stimulation (rTMS)

Considerations

- Reported success numbers
  - i.e. Goddard, et al 2009 reported 78% success with Neuromonics; but only 14 of initial 47 subjects completed the study
  - If 100 subjects enroll, but only 60 complete the study, and 40 of those 60 are successful, what is the success rate, 66%, or 40%?

- Research design
  - Risk of bias assessment tools consist of five domains: population, outcome, exposure, statistical analysis, and, for Random Control Trials, randomization, blinding, and withdrawals

Methodological risk of bias criteria of randomized controlled trials for the sound technology interventions

Evaluation and Treatment of Tinnitus: A Comparative Effectiveness Review; Pichora-Fuller, et al, in press
Counseling approaches

Tinnitus Retraining Therapy
(Jastreboff, Hazell)

• directive counseling
• modified version of Pavlovian extinction
• (also incorporates sound therapy)

Similarities of tinnitus with pain

• subjective
• invisible
• affected by extraneous events
Cognitive-Behavior Therapy
(Beck, Meichenbaum)

- The therapeutic effort to modify maladaptive thoughts and behaviors by applying systematic, measurable implementation of strategies designed to alter unproductive actions
- CBT gives patients hypotheses that can be self-tested
- Focuses on using a wide range of strategies to help clients overcome maladaptive thoughts and behaviors
  - Cognitive restructuring, dissociation of negative emotional association, attention directing, modification of avoidance behavior, journaling, role-playing, thought stopping, relaxation techniques, and mental distractions, coping strategies

Cognitive behavioral approaches ....

- Are designed to identify the unwanted thoughts and behaviors hindering natural habituation, challenge their validity, and replace them with alternative and logical thoughts and behaviors.
- The objective is to remove inappropriate beliefs, anxieties and fears and to help the patient recognize that it is not the tinnitus itself that is producing these beliefs, it is the patient's reaction (and all reactions are subject to modification).

The basic processes in cognitive-behavioral "intervention" are:

- Identify behaviors and thoughts affected by the tinnitus;
- List maladaptive strategies and cognitive distortions currently employed;
- Challenge the patient to identify negative thoughts;
- Identify alternate thoughts, behaviors, and strategies.

Differences between TRT and Cognitive Approaches (CA)

- CA are intensive and collaborative; designed for 8-12 weekly sessions and direct testing of hypotheses
- TRT uses directive counseling with 4-6 sessions over 18 month period
- CBT acts on high loop
- TRT deals with subconscious, lower loop
Concerns

- CA increase realistic, logical and rational thinking, relieves distress, and reduces maladaptive behaviors, but it does not call for the use of sound enrichment, though practitioners have noted that success using CA, such as CBT, may be enhanced when amplification is employed.

- Initially, while some patients recognize that certain thoughts are not rational or healthy, simply becoming aware of these thoughts does not make it easy to stop having them. It is important to note that CBT does not just involve identifying these thought patterns, it also involves replacing them with alternatives.

- In addition, CBT is typically delivered by psychologists, who may not have an understanding of the nature of the ear or impaired auditory system.

• Henry and Wilson, 2001 “encourage audiologists to adopt CBT” and have written a book for audiologists promoting this effort


Concerns

- TRT may require as much as 18 – 24 months of less active participation, and does not teach coping strategies or address emotional issues, (despite the fact that as many as 40% of tinnitus patients suffer from anxiety or depression).

- TRT suffers from lack of methodological confirmation (i.e. no treatment waiting control groups)

Sample of reported success rates for counseling approaches

- TRT (84% Sheldrake, Jastreboff, and Hazell)
- CBT (84%) vs 22% of controls – Zenner et al, 2012
- Biases: nearly all large studies reported by strong advocates of either TRT or CBT

Cochrane Reviews

- TRT
  - Only one study, involving 123 participants, matched the inclusion criteria for this review (five were excluded because they used a “modified” version). Although this study suggested considerable benefit for TRT in the treatment of tinnitus the study quality was not good enough to draw firm conclusions.
  - Phillips, McPherran, 2010
- CBT
  - Found no evidence of a significant difference in the subjective loudness of tinnitus.
  - However, found a significant improvement in depression score (in six studies) and quality of life (decrease of global tinnitus severity) in another five studies, suggesting that CBT has a positive effect on the management (reduction of annoyance and distress) of tinnitus.
  - Martinez-Devesa, et al 2010

Combination therapies

- No significant enhancement on the effects of CBT with the use of a low level white-noise generator
  - Hiller, 2005
- TRT was equally effective with sound generator or open ear hearing aids
  - Parazzini, 2011
Four aspects of tinnitus that should be addressed

- auditory
- attention
- emotional
- impact on sleep

Influence of noise and stress on probability of having tinnitus

- \( N = 12,166 \); \( N \) with tinnitus) = 2,024 (16%)
- Each year of age increased the odds ratio of tinnitus by about 3%.
- Men generally showed a higher risk for tinnitus compared with women.
- Exposure to noise and stress were important for the probability and level of discomfort from tinnitus. However, for the transition from mild to severe tinnitus, stress turned out to be more important.
- Reduction of likelihood of tinnitus if noise is removed = 27%, if stress is removed =19%), if both removed = 42%.
- Conclusions: Stress management strategies should be included in hearing conservation programs, especially for individuals with mild tinnitus who report a high stress load.
  - Baigi, et al; Ear and Hearing 2011. 32, 6:787-789

Tinnitus and Insomnia

- Severity of TRQ was shown to be a good predictor of sleep disturbance and of group association, especially the “emotional” subscore component (sensitivity 96.9% and specificity 55.3 % for identifying tinnitus patients with insomnia).
- The greater the insomnia disability, the more severe the patient’s complaints were regarding the tinnitus
Alternative Approaches

- **Mindfulness Based Stress Reduction (Kabat-Zinn)**
  - moment-to-moment non-judgmental awareness
  - includes continuous, immediate awareness of physical sensations, perceptions, affective states, thoughts, and imagery.

- **Progressive Tinnitus Management (Henry, et al)**
  - hearing aids, masking, TRT, and CBT.
  - key features are that it is a stepped-care approach, (telephone screen, informational counseling, intake assessment, treatment, extended treatment) leading to self efficacy

- **Combined directive / personal adjustment (Sweetow, Jeppesen; Kuk)**
  - Widex Zen Therapy (disclosure)
  - also includes relaxation exercises, sleep management, sound therapy

WZT in relation to TRT and CBT

- WZT emphasizes a collaborative interaction versus directive counseling (more similar to CBT in this regard)
- WZT emphasizes flexibility with multiple components
- WZT more short term (with greater load in front (coincident with amplification))
- WZT more active in counseling aspects, passive in sound therapy
- WZT aims to help patient develop coping strategies (TRT considers this a potential distraction from main goal of habituation and may encourage patient to search for better ways of making reactions "not as bad")
- A critical segment of WZT is relaxation and sleep management (not part of TRT), but can be considered adjunctive approaches
- CBT does not require sound therapy
- WZT is constantly evolving, it is not static!

Current sound treatments

- Maskers
- Noise generators
- Music (unfiltered, filtered, fractal)
- Hearing aids (effective in over 60% of cases)
  - McNeill, et al. (2012) 70 patients: 26 reported their tinnitus was totally masked, 28 reported partial masking (i.e., 77 percent, or 54 of 70 reported partial or total masking);16 reported no masking.
- Combination instruments
- Home based sounds
- CDs/internet
Why hearing aids may help tinnitus patients

- Greater neural activity allows brain to correct for abnormal reduced inhibition
- Enriched sound environment may prevent maladaptive cortical reorganization
- Alter production peripherally and/or centrally
- Reduce contrast to quiet
- Partially mask tinnitus
- Fatigue and stress is reduced allowing more resources to be allocated to tinnitus fight
- All of the above may facilitate habituation and
- The majority of tinnitus sufferers have at least some degree of hearing loss

Patterned sound therapy (Reavis and Zeng, 2011)

- MP3 player emitting an amplitude or frequency modulated pulsing signals
- Good results, especially with electrical stimulation
- More "cortically interesting"?
- Problem: limited research
- Marketed as Sound Cure “Serenade”

Coordinated reset stimulation (Tass, 2011)

- uses sounds to desynchronize neural firing (on the assumption that the tinnitus percept is related to pathological neural synchrony), as opposed to trying to suppress neuronal firing or alter neural plasticity patterns.

Sound Therapy Synergy

- Spectrally “activated” classical music combined with multi-sensory exercises to enhance neural plasticity
- Marketed for “tinnitus, hyperacusis, dizziness, CAPD, figure-ground discrimination, anxiety, sleep disorders, ear pressure, speech problems, and more”
Changing concepts

- Jastreboff said “don’t mask”
- Tyler said “not so fast”
- Newman and Sandridge: consider cost effectiveness.....

Confused?
What are the objectives of sound therapy?

- Complete masking
- Partial masking
- Mix
- Habituate
- Distract
- Suppress

Issues relating to sound therapy

- Intensity Level
- Spectral characteristics
- Dynamic characteristics (modulation)
- Temporal factors

- Music has been shown to activate the limbic system and other brain structures (including the frontal lobe and cerebellum) and has been shown to produce physiologic changes associated with relaxation and stress relief.
YOUR BRAIN ON MUSIC

The brain at rest

The brain's reaction to music

WHERE IS MUSIC PROCESSED?

Neuromonics

- a bit of cognitive therapy
- a bit of TRT
- Music therapy (for affect and relaxation) and wide band stimulation using an iPod-like processor with Bang and Olufsen earphones
- Rhythm
- Hearing instrument algorithm (equal sensation level) for hearing loss compensation
- 2 stage program
Comparison of sound generators (SGs) vs Neuromonics tinnitus treatment (NTT)

N= 56; 6 month trial

Both groups (SG and NTT) demonstrated a significant reduction in tinnitus for SG and NTT. However, there were no differences in the SG or NTT treatment groups.

Conclusions: Both protocols (SG and NTT) yielded significant improvements with regard to quality of life (HRQoL) issues, based on the THI improvements

SG appears to be more cost-efficient than NTT. "The cost per unit of improvement (treatment utility) on the THI (scale from 1-100 points) measured in "quality-adjusted life years" was $604 per point for the sound generator treatment compared to $1,771 per point for the Neuromonics treatment. The implication here is that equivalent gains might be obtained at a lesser cost to the patient."


Target processing

1 octave notch around Tinnitus frequency.
Same processing on both ears

Placebo processing

1 octave notch elsewhere
No notch at tinnitus frequency

Okamoto H et al. PNAS 2010;107:1207-1210

Selecting the right sounds

Sounds (including music) affects people in different ways, due to inherent, learned (and cultural) preferences

Thus it is appropriate to use relaxing background sounds (that activate the parasympathetic division of the autonomic nervous system) and minimize exposure to alerting, negative, or annoying sounds (that activate the sympathetic division)

Earworms?
Earworms

- Nearly 98% of people have had songs stuck in their head, Kellaris reported at the recent meeting of the Society for Consumer Psychology. The 559 students – at an average age of 23 – had lots of trouble with the Chili’s “Baby Back Ribs” jingle and with the Baha Men song “Who Let the Dogs Out.” But Kellaris found that most often, each person tends to be haunted by their own demon tunes.

- “Songs with lyrics are reported as most frequently stuck (74%), followed by commercial jingles (15%) and instrumental tunes without words (11%),” Kellaris writes in his study abstract. “On average, the episodes last over a few hours and occur ‘frequently’ or ‘very frequently’ among 61.5% of the sample.”

- Top 10 earworm list:
  - Chili’s “Baby Back Ribs” jingle.
  - “Who Let the Dogs Out”
  - “We Will Rock You”
  - Kit-Kat candy-bar jingle (“Gimme a Break...”)
  - “Mission Impossible” theme
  - “YMCA”
  - “Whoop, There It Is”
  - “The Lion Sleeps Tonight”
  - “It’s a Small World After All”

Zen fractal tones

- An optional listening program in certain (Passion, Mind, Clear, and Dream) Widex hearing aids that plays adjustable, continuous, chime-like tone complexes using fractal algorithms.

- The chimes are generated based on an understanding of the properties of music that would be most relaxing (Robb et al., 1995):
  - Ability to self select music.
  - Tempo near or below resting heart rate (60-72 bpm).
  - Fluid melodic movement.
  - Variety of pitches
  - No rapid amplitude changes
  - Element of uncertainty (Beauvous 2007)
  - Passive listening

Frequency response and amplitude settings are based on in situ audiogram.
A filtered broad band noise can be used as a separate program or in combination with the fractal tones.
Signals are distant.
Summary of findings

- Fractal tones were effective as a tool in promoting relaxation and reducing annoyance from tinnitus
- Both fractal tones and noise reduced tinnitus annoyance, but the fractal tones were preferred by subjects for longer term use

Limitations with some studies

- Stimulus presentations lasted only for seconds
- Studies done in a sound booth
- Hearing loss amongst subjects vary
- TDH 50s, which have significantly reduced amplitude from ~7-13KHz, might be used
Does acoustic therapy help?

- Herraz, et al, 1999
  - Counseling only; 94% showed “improvement” (N ~ 30)
  - Counseling with hearing aids; 85% showed “improvement” (N ~ 35)
  - Counseling with sound generators; 83% showed “improvement” (N ~ 30)

- McKinney, et al; 1999
  - Counseling only; 72% showed “improvement” (N=54)
  - Counseling with sound generators at just audible level; 75% showed “improvement” (N=72)
  - Counseling with hearing aids; 61% showed “improvement” (N=56)
  - Counseling with sound generators at mixing level; 83% showed “improvement” (N only 36)

Cochrane Review

- Sound Generators:
  - The limited data from the included studies failed to show strong evidence of the efficacy of sound therapy in tinnitus management.
  - The absence of conclusive evidence should not be interpreted as evidence of lack of effectiveness.
  - “The lack of quality research in this area, in addition to the common use of combined approaches (hearing therapy plus counseling) in the management of tinnitus are, in part, responsible for the lack of conclusive evidence.
    - (Hobson, Chisholm, El Rafaie, 2010)

Reported success rates for acoustic therapies

- Neuromonics: 48% (Goddard, et al) – 91% (Davis, et al)
- Fractal tones plus amplification: 57% (Sweetow and Henderson-Sabes) - 90% (Henzfeld)
- Biases: most studies reported by researchers with conflicted interests
- Maskers (60-84%)
- Sound Cure (S-Tones) are four times more likely to provide relief than white noise; 35% of patients experienced 70% or better reduction in tinnitus perception: 35% experienced 30-50% reduction; 30% saw less than 30% reduction; Reavis, et al; 2012 – “independent study at UC Irvine”
Parallel vs serial approaches

• Tinnitus activation is parallel  
• Music processing is parallel  
• Treatment should be parallel...failure with serial approach may leads to activation of “failure” circuitry in rostral anterior cingular cortex, striatum, caudate nucleus, etc.  
• Humans want immediate gratification.  
• An interesting study....success rate of “first-timers” vs. repeat patients.  
• And, is the success or failure of certain therapies related to the extent to which the tinnitus has permeated physiologic and cognitive aspects?

So what works?

• Meta-analytic reviews indicate that there is an approximate 70% success rate with counseling alone  
• Adding sound therapy brings success rate into or above the 80% level  
  • Any of the “reasonable” approaches, depending on the “skills” of the audiologist or therapist

An even better question.....

• What constitutes success?  
  — Improvement on THI, TRQ, TFI?  
  — Reduction in loudness?  
  — Improvement in QOL?  
• Benefit does not equal satisfaction!!!!!!!

• Does dogma hurt our goal?
No one is exempt from talking nonsense;

the only misfortune is when one does it solemnly

Thanks for listening

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