A meta analysis of tinnitus theories and treatments reveals a wide array that are often diametrically opposed.

- Yet, evidence exists verifying effectiveness and correctness of each.
- For example, one music therapy amplifies the frequency region of hearing loss while another attenuates that region.
- Can both be correct, or are both incorrect.
- How can they both co-exist?

Recap of theories of tinnitus origin (with apologies to the many whose contributions I omitted)
Proposed peripheral mechanisms

- Ion channel regulation for excitability of neurons
- Calcium induced changes in intra or extracellular processes
- Discordant damage to outer and inner hair cells resulting in increased spontaneous activity; Jastreboff, 1990; Cherry-Croze, Truy, and Morgan, 1994
- Damaged outer hair cells cause excessive release of glutamate from inner hair cells resulting in sustained cochlear activity; Patuzzi, 2002
- Imbalance of afferent and efferent:
  - Deficient afferent neurotransmitter glutamate at the cochlear-8th nerve synapse
  - "disinhibition" from neurotransmitters such as gamma aminobutyric acid (GABA)

Brainstem origin

- Increased activity at higher levels due to decreased inhibition of DCN and additional disinhibition at IC, related to diminished GABA activity (Brummett; Moller; Salvi)
- Hyperactive spontaneous activity in dorsal cochlear nucleus; (Kaltenbach, 2000)
- Hyperactivity in inferior colliculus and dorsal cochlear nucleus reorganize tonotopic maps; (Salvi, Wang, and Powers)

Cortex

- Hyperactivity of left transverse temporal gyrus; (Arnold, Bartenstein et al, 1996)
- Abnormal activation of auditory cortex and amygdala; (Lockwood et al, 1998)
- Cortical reorganization following peripheral damage resulting in over-representation of frequencies at upper and lower borders of hearing loss; (Salvi, Lockwood and Burkard, 2000; Engineer and Kilgard, 2010)
Tinnitus is associated with abnormal EEG-patterns, showing enhanced activity in the δ band and reduced activity in the α band (Weisz, Moratti, Meinzer, Dohrmann, & Elbert, 2005). MEG indicates that subjects with tinnitus < 4 years have gamma network predominantly in the temporal cortex; but subjects with tinnitus of a longer duration show a widely distributed gamma network into the frontal and parietal regions (deRidder, 2011).

Other likely (non-auditory) mechanisms

- Correlated activity across nerves by phase locking - ephaptic transmission
- Extralemniscal neurons, particularly in dorsal cochlear nucleus and AII area, receiving input from somasthetic system
- Sensory remodeling in the central auditory system
- Association with fear and threat (limbic system)

Psychological contributions

- Habituation: intolerance results from individual’s failure to adapt (Hallam et al, 1984; 2006)
- Attention: failure to shift attention away from tinnitus (Hallam and McKenna, 2006)
- Enhanced tinnitus perception is learned response resulting from “negative” emotional reinforcement involving limbic system and autonomic activation (Hallum; Jastreboff and Hazell, 1993; McKenna, 2004) de-emphasizes connection with peripheral hearing loss
Summary of modern theories of tinnitus origin

- 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 (afferent) function
- Over-representation of edge-frequencies (cortical plasticity)
- Other somatosensory influences (Cervical disturbances, TMJ, etc.);
  Correlated activity across nerves by phase locking - ephaptic transmission
- Extralemniscal neurons, particularly in dorsal cochlear nucleus and AII area, receiving input from somasthetic system
- Association with fear and threat (limbic system)
- Increased attention related to limbic system involvement
- Dysfunctional gating in basal ganglia or thalamic reticular nucleus

Models based on peripheral measures ..........

- fail to predict completely percept laterality
  • Role of CNS adaptation (neural plasticity?)
- Absolute and relative depth of hearing loss are uncorrelated to percept severity
  • Role of CNS emotional binding (limbic system)

Tsai, Cheung, and Sweetow, Laryngoscope; 2012 (in print)

Lack of correlation between tinnitus severity and auditory threshold

Tsai, Cheung, and Sweetow, Laryngoscope, 2012 (in print)
Questions requiring more clarification

- Why don’t all hearing impaired individuals have tinnitus; for example, why do only 20-40% of persons with noise induced hearing loss have it; is it blocked sub-cortically?
- Based on discordant damage theory, shouldn’t the largest group of tinnitus patients have a ~50 dB loss?
- Do the 36% of tinnitus patients who have normal hearing, all have undocumented OHC damage? Why don’t OAEs show this?
- Why can’t we accurately predict laterality percept?
- Why is tinnitus merely a minor distraction for 80%?
- Why can’t we “counsel away” abnormal autonomic nervous system activation for more patients?
- Why do so many patients report intermittent or fluctuating tinnitus?
- Why do some people have “reactive” tinnitus?

Inspiration

63 year old otolaryngologist with 40 year history of mostly constant, high-pitched tinnitus. Tinnitus was mostly louder in the left ear, with episodic increases in loudness. Audiogram showed right moderate and left moderate-to-severe sensorineural hearing loss.

Left hemispheric stroke involving “the more dorsal part of the corona radiata. In addition there is involvement of the neostriatum, including the body of the caudate and the caudodorsal aspect of the putamen.”

Tinnitus Disappeared Completely Hearing Remained Unchanged

Cheung and Larsen, 2010

Interpretation of 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, 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, 2011

Revised habituation model
(after Jastreboff and Hazell, 1993)

Tinnitus Therapies

- Reduce Contrast
- Mask Phantom Percept
- Suppress Hyperactivity
- Examples:
  - Hearing aids
  - Neuromonics
  - Fractal tones
  - Cochlear implants

- Reclassify Phantom Percept
- Reduce Salience
- Mitigate Emotional Distress
- Examples:
  - Tinnitus retraining
  - Neuromonics
  - Fractal tones
  - Antidepressants
  - Cognitive-behavioral therapy
  - MBSR

- Disrupt Information Conveyance
- Avoid Interference with Audition
- Examples:
  - Striatal Neuromodulation
  - Vagal nerve stimulation
  - Cortical Stimulation (rTMS)

Auditory-Striatal-Limbic Connectivity

Dashed lines represent neural interpretation of tinnitus percept.
Disclosure

• Consultant for Widex

Reversing pathological neural activity using targeted plasticity

• Several studies have reported that the severity of chronic pain and tinnitus is correlated with the degree of map reorganization in somatosensory and auditory cortex, respectively.

• Repeatedly pairing tones with brief pulses of vagus nerve stimulation completely eliminated the physiological and behavioral correlates of tinnitus in noise-exposed rats. Improvements persisted for weeks after the end of therapy.

• Pairing release of neuromodulators (such as acetylcholine and norepinephrine) with tones that are distant from the tinnitus frequency reverse the frequency map distortion and the pathological activity patterns associated with tinnitus.


Three aspects of tinnitus that may be bothersome

• auditory
• attentional
• emotional
**“Reasonable” tinnitus patient management procedures by audiologists**

- Counseling
  - Reassurance (including placebo)
  - Education
  - Cognitive-Behavioral Therapy

- Sound enrichment
  - Masking or mixing
  - Amplification

- Combination
  - Desensitization / Habituation (TRT)
  - Acoustic desensitization protocol (Neuromonics)
  - Fractal Tones (Zen)

**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

**Goals**

- Active listening (distraction)
- Masking (covering up)
- Passive listening (habituation, desensitization)
Preference for tinnitus “masking” sounds

- Music = 87.8%
- Relaxation (soft music with instruction) tapes = 7.3%
- Silence or no masker = 4.9%
- Pure tones = 0%


Conclusions of Kochkin, et al; 2011

- Of the nine tinnitus treatment methods assessed, none were tried by more than 7% of the subjects.
- Treatment methods rated with substantial tinnitus amelioration were hearing aids (34%) and music (30%).
- Subjects who had their hearing aids fit by professionals using comprehensive hearing aid fitting protocols are nearly twice as likely to experience tinnitus relief than respondents fit by hearing care professionals using minimalist hearing aid fitting protocols.
- This study confirms that the provision of hearing aids offers substantial benefit to a significant number of people suffering from tinnitus. This fact should be more widely acknowledged in both the audiological and medical communities.

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.
“Rules” of music and emotions

- Slow onset, long, quiet sounds – calming
- Music with a rhythm slower than your natural heart rate (60 – 72 beats per minute) is useful to many people
- Repetition is emotionally satisfying

Neuromonics

- A bit of cognitive therapy
- A bit of TRT directive counseling
- Music therapy (for affect and relaxation) and wide band stimulation using an iPod-like processor with Bang and Olufsen earphones
- Rhythm, melody
- Hearing instrument algorithm (equal sensation level) for hearing loss compensation
- 2 stage program
- Does not provide amplification outside of 2-4 hour daily use

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).

Cultural preferences

Earworms?

Definition of fractal

- "a rough or fragmented geometric shape that can be split into parts, each of which is (at least approximately) a reduced-size copy of the whole"

- Properties include self-similarity and a simple and recursive definition

Fractals in nature

- Examples include:
  - clouds, rivers, fault lines, mountain ranges, craters, snowflakes, crystals, lightning, cauliflower, broccoli, blood vessels, ocean waves and DNA
• Fractal tones create a melodic chain of tones that repeat enough to sound familiar and follow appropriate rules, but vary enough to not be predictable.

• Fractal technology ensures that no sudden changes appear in tonality or tempo.

Conclusion of Sweetow and Sabes, 2010

• 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.

Sweetow & Henderson-Sabes, The use of acoustic stimuli in tinnitus management. JAAA 21,7, 461-473, 2010

A meta analysis of tinnitus theories and treatments reveals a wide array that are often diametrically opposed.

• Yet, evidence exists verifying effectiveness and correctness of each.

• For example, one music therapy amplifies the frequency region of hearing loss while another attenuates that region.

• Can both be correct, or are both incorrect.
How can they both co-exist?

Mechanisms

<table>
<thead>
<tr>
<th>Mechanisms</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vagal nerve stimulation</td>
<td>works because it reverses neural reorganization that occurs, but should not occur.</td>
</tr>
<tr>
<td>Cheung and Larsen</td>
<td>claim tinnitus occurs due to improper gating at the basal ganglia.</td>
</tr>
<tr>
<td>Rauschecker cites the thalamic reticular nucleus as an aberrant gateway.</td>
<td></td>
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<tr>
<td>Cerebellar malfunction may be related to tinnitus (Bauer)</td>
<td></td>
</tr>
<tr>
<td>Abnormal alpha-beta wave ratios (Weisz)</td>
<td></td>
</tr>
<tr>
<td>Increase in CNS activity (Kaltenbach, et al; Eggermont, et al)</td>
<td></td>
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<tr>
<td>Abnormal gamma wave activity (DeRidder)</td>
<td></td>
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<tr>
<td>Decrease in CNS activity (Liberman and Kiang, 1978)</td>
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</tbody>
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Treatments

<table>
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<tbody>
<tr>
<td>Neuromonics uses music filtered to stimulate hearing loss regions.</td>
<td>Okomoto notches in regions where there is hearing loss to drive neural plasticity.</td>
</tr>
<tr>
<td>Zen fractal tones use unpredictable music</td>
<td>Neuromonics uses a closed set of pre-recorded songs</td>
</tr>
<tr>
<td>Neuromonics uses pre-recorded music that relaxes via active listening</td>
<td>Zen fractal tones expound the virtues of unpredictability</td>
</tr>
<tr>
<td>TRT suggests avoiding silence and encourages sound enrichment 24-7.</td>
<td>Neuromonics suggests 2-4 hours per day</td>
</tr>
<tr>
<td>CBT uses distraction techniques.</td>
<td>Mindfulness based stress reduction encourages the patient to embrace the tinnitus.</td>
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</table>
Which work?
Which provide immediate relief?
Which provide long term relief?

- They all work
- Maskers, amplification, Zen fractals, rTMS may provide immediate relief (analogous to pain medication)
- MBSR, TRT, Zen fractals may provide long term relief (analogous to physical therapy or behavioral modification)
- This is why we may need both, a phased in, comprehensive, holistic strategy.

Parallel vs serial approaches

- Tinnitus activation parallel
- Music processing 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?

Thanks for listening
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