Research-based Tinnitus Treatments

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CHRISTCHURCH NEW ZEALAND

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Journal of Neuroscience Methods

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Clinical Neuroscience

Feasibility study of a game integrating assessment and therapy of tinnitus

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Tinnitus & treatment realities

- Heterogeneous with regards to the underlying cause & phenotype
- Few specialized treatment centres
- Relatively low evidence for many diagnostic & therapeutic procedures
- Those treatment recommendations that do exist, are not always feasible or fulfilled in clinical practise
- Identification of sub-types suggests high relevance for treatment recommendations
- Treatment highly variable – across & within disciplines (audiology, ENT, psychology/psychiatry) but also across & within countries.

(Schecklmann, et al., 2012; Langguth, et al., 2011; Hoare, et al., 2012)

J Am Acad Audiol 25:106–125 (2014)

Review

Experimental, Controversial, and Futuristic Treatments for Chronic Tinnitus

DOI: 10.3766/jaaa.25.1.7

Robert L. Folmer*†
Sarah M. Theodoroff*†
William Hal Martin†
Yongbing Shi†‡

Robert L. Folmer, Ph.D., National Centre for Rehabilitative Auditory Research, Portland Veteran's Administration (VA) Medical Centre, USA

- Acknowledged heterogeneity of studies reviewed & difficulty this poses on a precise meta-analysis
- "Not meant to be an exhaustive review; the article reflects the authors' professional biases and prerogatives" *(Folmer, et al., 2014; p. 107)*
- Provides information on a wide range of approaches

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INVASIVE: Scant support, potentially harmful & "tinnitus is a non-life threatening symptom"

NON-INVASIVE: Support for efficacy of hearing aids, types of environmental sound enrichment, CBT, counselling, hypnosis, biofeedback & relaxation training

OVER-THE-COUNTER / PRESCRIPTION MEDICATION(S): Anti-depressants, anti-anxiety, obsessive-compulsive control

CLINICAL TRIALS: Require "Effectiveness above & beyond the placebo effect" *(Folmer, et al., 2014; p. 106)*

J Am Acad Audiol 26:595–597 (2015)

Letter to the Editor

DOI: 10.3766/jaaa.14041

All Treatments in Tinnitus Are Experimental, Controversial, and Futuristic: A Comment on "Experimental, Controversial, and Futuristic Treatments for Chronic Tinnitus" by Folmer et al (2014)

Dirk De Ridder,
Department of Surgical Sciences, Unit of Neurosurgery, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand; and Tinnitus Research Initiative

Sven Vanneste
Laboratory for Auditory and Integrative Neuroscience, School of Behavioural and Brain Sciences, University of Texas

Ana Belen Elgoyhen
Instituto de Investigaciones en Ingeniería Genética y Bilogía Molecular, Dr. Héctor N. Torres, Consejo Nacional de Investigaciones Científicas y Técnicas, Buenos Aires, Argentina; Departmento de Farmacología, Facultad de Medicina, Unversidad de Buenos Aires, Buenso Aires, Argentina; and Tinnitus Research Initiative

Berthold Langguth, B., de Nora, M. (2015)
Department of Psychiatry and Psychotherapy, Interdisciplinary Tinnitus Clinic, University of Regensburg, Regensburg, Germany; and Tinnitus Research Initiative

Matteo de Nora
Tinnitus Research Initiative

(Folmer, et al., 2014)

Make a distinction between:

Tinnitus treatments considered established & evidence based

Experimental, controversial (non-evidence based) & futuristic

(de Ridder et al., 2015; p. 595)

- "…the authors [Folmer et al., 2014], suggest most patients can be treated with the established treatments in a satisfactory way"
- Considering the evidence base, both the distinction (between established versus experimental) & the assertion that established treatments are satisfactory – are not correct
- "…same criteria should be used to judge the scientific evidence behind the effectiveness of different treatments"
- This highlights that some therapies considered established, currently have a low, high-quality trial evidence of efficacy (e.g., hearing aids – *Hoare, et al., 2014*)
- Yet, "evidence for some treatments [they] consider as controversial/experimental is not that low" (e.g., rTMS – *Anders, et al., 2010; Khedr, et al., 2009; Marcondes, et al., 2010*)

Recommendations

- Precise description of all clinical features of tinnitus in a given individual, based on reliable & validated assessment instruments
- Good, reliable clinical characterization tinnitus as a prerequisite for arriving at a clear diagnosis, enabling appropriate treatment
- Individualised patient outcome assessments – to determine whether treatment resulted in improvement in areas most relevant for the patient/client
- Standardised assessment methods – for comparison of results across centres, clinic audits, & epidemiological studies
- Analysis of therapies, interventions (clinical trials, systematic clinical observations) using standardised assessments at defined intervals: before, during, & after intervention.

(Langguth, et al., 2011; Hoare, et al., 2014)

Case history

- **Information, self-help materials**
- Manual *(Konzag, et al., 2006)*
- **Scope of practise**
- **Consider specialist practitioner networks of those accommodating tinnitus (multidisciplinary)**
  - ENT (*Langguth, et al., 2011)*
  - Counselling/psychological *(Searchfield, et al., 2010)*
  - Musculoskeletal *(Sanchez & Rocha, 2011)*
  - Jaw *(Sanchez & Rocha, 2011)*
  - Sleep *(Kentish, Crocker & McKenna, 2000; Hébert & Carrier, 2007)*
  - Relaxation *(Öst, 1987; Weber, et al., 2002)*

(Langguth, et al., 2011)

Themes

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- Internet strategies
- Medical Management
- Non-invasive Neurological Methods
- Psychological & Counselling Therapies
- Sound Provision
- Self-help & Pervasive Healthcare Approaches
- Neuroplasticity & Training Models

Internet strategies

- Uppsala (Sweden) Treatment Programme

Internet-Based Cognitive Behavioral Therapy for Tinnitus

▼

Gerhard Andersson and Viktor Kaldo
Uppsala University

(Andersson & Kaldo, 2004)

Professor of Psychology Linköping University & CBT-trained Psychotherapist

AWARDS:

Outstanding Swedish psychologist (2014)
Nordic prize in medicine (2014)
Swedish Assoc. of Behaviour Therapy, Lifetime achievement award (2015)

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BTA BRITISH TINNITUS ASSOCIATION

ATA

TINNITUS ASSOCIATION Victoria

Tinnitus Research Initiative
Together for a Cure

AMERICAN TINNITUS ASSOCIATION

audiology australia

Table 1
Overview of Self-Help Treatment for Tinnitus Presented via the Internet

Case Formulation
Structured clinical interview (in clinic)
Internet-based questionnaire assessment
Treatment rationale and information (in session and on the Web)
Treatment Presented in Six Separate Modules*
Applied relaxation (1. progressive relaxation, 2. short progressive relaxation, 3. cue-controlled relaxation, and 4. rapid relaxation)
Positive imagery
Sound enrichment by means of external sounds
Hearing tactics and advice regarding noise sensitivity
Modification of negative thoughts and beliefs
Behavioral sleep management
Advice regarding concentration difficulties, exercises of concentration (mindfulness)
Exposure to tinnitus
Advice regarding physical activity
Relapse prevention
Follow-Up
Internet-based questionnaire assessment

*Treatment also includes continuous interaction with the therapist and training diaries.

(Andersson & Kaldo, 2004)

Pros & Cons

- Promotes regular interaction, assessment – works with individual lifestyle; remote access
- Supports monitored group approaches
- Fosters programme adherence

- Single case-based study
- Case formulation & pathway may need to be changed & this is readily facilitated in a 1:1 setting, but not as straightforward with internet
- Not appropriate for all
- Should follow (not replace) professional/specialist consultation & receive appropriate review

(Andersson & Kaldo, 2004)

A Randomized Controlled Trial of Internet-Delivered Cognitive Behavior Therapy and Acceptance and Commitment Therapy in the Treatment of Tinnitus

(Hesser, et al., 2012)

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METHODS:

- *n* = 99, (mean age 48.5 years; 43% female)
- CBT (*n* = 32)
- Acceptance & Committment Therapy (*n* = 35)
- Control (monitored Internet discussion forum; *n* = 32)

RESULTS:

Mixed-effects linear regression analysis of all randomized participants showed significant effects on the primary outcome (Tinnitus Handicap Inventory) for CBT & for ACT compared with controls at post-treatment

Within-group effects were substantial from pre-treatment through 1-year-follow-up for both treatments; no significant difference between treatments

CONCLUSIONS:

ACT procedures may be a viable alternative to traditional CBT techniques in the management of tinnitus. The Internet can improve access to psychological interventions for tinnitus

Other studies

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(Kaldo, et al., 2008)

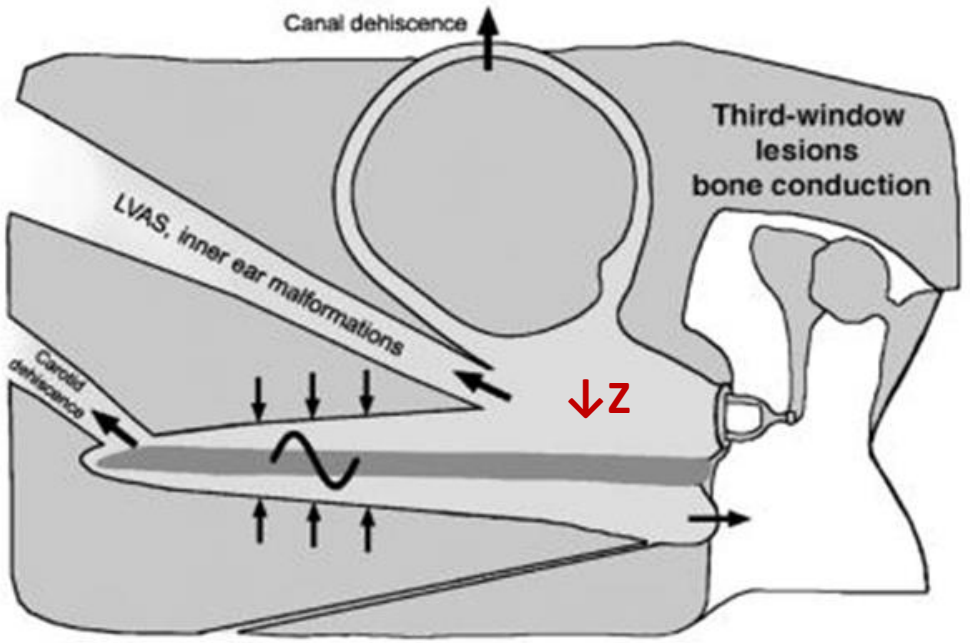
- 'Randomized controlled trial' comparing internet-based, self-help (*n* = 26) with group-based CBT (*n* = 25)
- Significant improvements for both groups, little difference between the groups, results stable after 1-year follow-up
- Consumed less time & 1.7 times more cost-effective
- However, intake rating that internet-approach less credible

(Abbott, et al., 2009)

- Industrial, 'cluster randomized trial' comparing internet-based, CBT program (n = 28) for tinnitus distress compared to information-only controls (n = 23)
- Internet CBT was not significantly better than controls, but high attrition & resultant low sample size, precluded generalising findings
- Internet programme needs to be engaging to ensure compliance

Medical Management

- Glomus Tumour;
- Otosclerosis
- Superior Semi-circular Canal Dehiscence
- Sudden Unilateral SNHL
- Vascular Compression
- Vestibular Schwannoma
- Ménière's



3rd Window Lesions, (BC) THEORY: 3rd Window causes ↓ impedance on SV side, improving cochlear response to BC. For patients with healthy cochleae as in SSCD, supra-normal BC thresholds may be seen.

Medical Management

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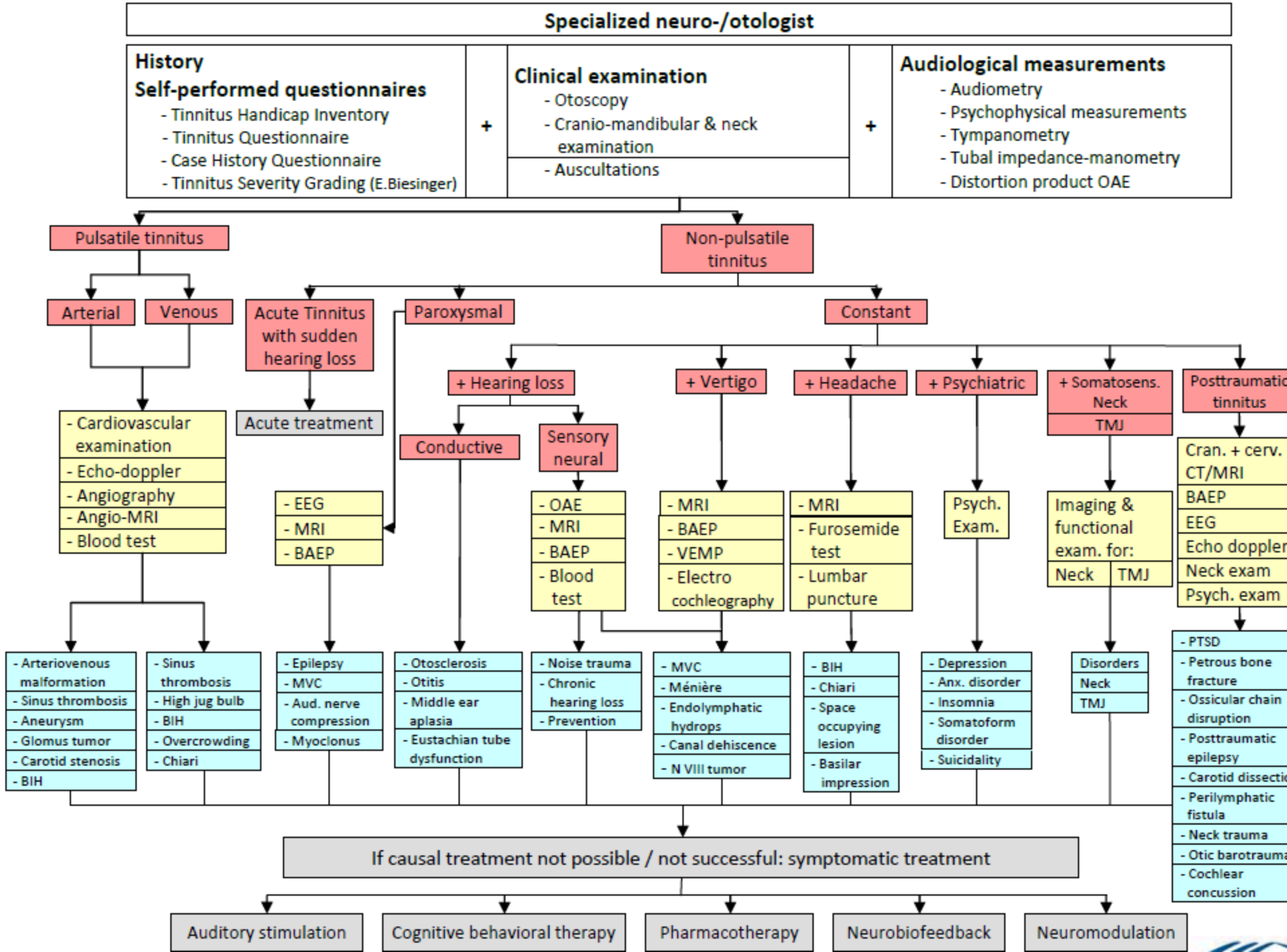
- Medical model – formal medical-based specialist assessment as initial step in diagnosis & treatment

- "…to standardize & improve clinical management of tinnitus patients, development of an algorithm for diagnostic & therapeutic tinnitus management (as a living, changing document)"

- Generated by a multidisciplinary team: otolaryngologists, neuro-otologists, audiologists, neurologists, psychiatrists & a neurosurgeon.

(Langguth, et al., 2011; Tinnitus Research Initiative, 2006)


Specialized neuro-/otologist
History
Self-performed questionnaires
- Tinnitus Handicap Inventory
- Tinnitus Questionnaire
- Case History Questionnaire
- Tinnitus Severity Grading (E.Biesinger)
+
Clinical examination
- Otoscopy
- Cranio-mandibular & neck examination
- Auscultations
+
Audiological measurements
- Audiometry
- Psychophysical measurements
- Tympanometry
- Tubal impedance-manometry
- Distortion product OAE
Pulsatile tinnitus
Non-pulsatile tinnitus
Arterial
Venous
Acute Tinnitus with sudden hearing loss
Paroxysmal
Constant
+ Hearing loss
+ Vertigo
+ Headache
+ Psychiatric
+ Somatosens. Neck
TMJ
Posttraumatic tinnitus
- Cardiovascular examination
- Echo-doppler
- Angiography
- Angio-MRI
- Blood test
Acute treatment
- EEG
- MRI
- BAEP
Conductive
Sensory neural
- OAE
- MRI
- BAEP
- Blood test
- MRI
- BAEP
- VEMP
- Electro cochleography
- MRI
- Furosemide test
- Lumbar puncture
Psych. Exam.
Imaging & functional exam. for:
Neck
TMJ
Cran. + cerv. CT/MRI
BAEP
EEG
Echo doppler
Neck exam
Psych. exam
- Arteriovenous malformation
- Sinus thrombosis
- Aneurysm
- Glomus tumor
- Carotid stenosis
- BIH
- Sinus thrombosis
- High jug bulb
- BIH
- Overcrowding
- Chiari
- Epilepsy
- MVC
- Aud. nerve compression
- Myoclonus
- Otosclerosis
- Otitis
- Middle ear aplasia
- Eustachian tube dysfunction
- Noise trauma
- Chronic hearing loss
- Prevention
- MVC
- Ménière
- Endolymphatic hydrops
- Canal dehiscence
- N VIII tumor
- BIH
- Chiari
- Space occupying lesion
- Basilar impression
- Depression
- Anx. disorder
- Insomnia
- Somatoform disorder
- Suicidality
Disorders
Neck
TMJ
- PTSD
- Petrous bone fracture
- Ossicular chain disruption
- Posttraumatic epilepsy
- Carotid dissecti
- Perilymphatic fistula
- Neck trauma
- Otic barotrauma
- Cochlear concussion
If causal treatment not possible / not successful: symptomatic treatment
Auditory stimulation
Cognitive behavioral therapy
Pharmacotherapy
Neurobiofeedback
Neuromodulation

Medications – treat or cause?

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Table 1. Examples of Medications Causing Tinnitus

Type of Medication	Examples	Tinnitus-Related Effects
Analgesics	Salicylates, nonsteroidal anti-inflammatory agents	Cause subjective and high-frequency tinnitus; may be reversible when the drug is stopped
Antibiotics	Aminoglycosides, e.g., gentamicin, streptomycin, neomycin. Other antibiotics such as erythromycin, azithromycin, vancomycin, tetracycline, and chloramphenicol.	Cause subjective and high-frequency tinnitus; not usually reversible
Antineoplastic agents	Bleomycin, cisplatinum, methotrexate, vincristine	Cause subjective and high-frequency tinnitus; not usually reversible
Loop diuretics	Bumetanide, ethacrynic acid, and furosemide	Cause subjective and high-frequency tinnitus; usually reversible when the drug is stopped
Others		
Quinine/chloroquine		Cause subjective and high-frequency tinnitus; transient and usually reversible
Tricyclic antidepressants	Amitryptilline, imipramine, doxepin	Cause subjective and high-frequency tinnitus; usually reversible when the drug is stopped

Anti-depressants, Anti-convulsants, Anxiolytics, Hypnotics, Tranquilizers
Interactions? Ability to metabolise?

(Holmes & Padgham, 2011; p. 99)

SNPs & Medication

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- **Single Nucleotide Polymorphism**,
- **Simple Nucleotide Polymorphism**,
- **SNP, “snip” or “snips” (plural)**

Genetic anomaly – DNA sequence variation occurring commonly within a population (e.g. 1%)

CYP2D6 is a gene polymorphism that encodes how people metabolise

People respond differentially to medications/drugs and can be high or low responders

(Kleim, 2015)

Non-invasive Neurological Methods

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- **Brain Stimulation**
  - TMS
  - rTMS
  - tDCS

Neuromodulation:

Changing pathological neuronal activity associated with tinnitus perception & sustainability

Neuromodulation techniques are theorised to work by inducing neural plasticity & disrupting aberrant neural networks responsible for tinnitus

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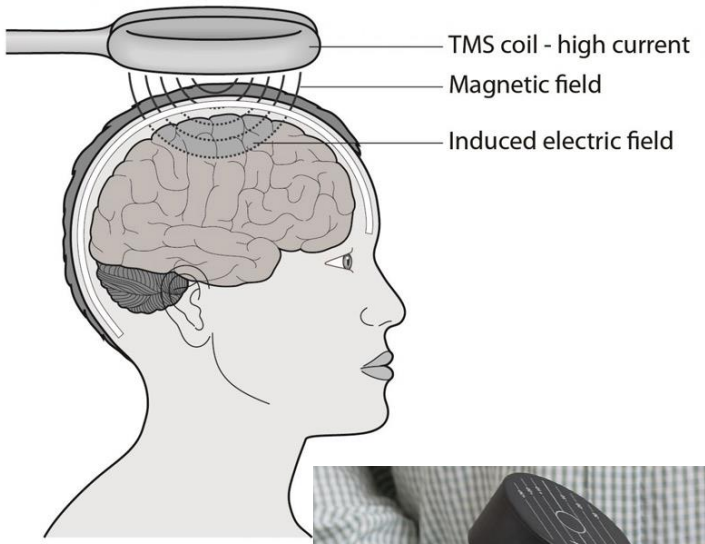
- rTMS: *(Anders, et al., 2010)* A randomized, placebo controlled study
- rTMS: (*Khedr, et al., 2009)* A one-year follow up of patients with chronic tinnitus
- *rTMS: (Marcondes, et al., 2010) A* double-blind controlled, clinical and neuroimaging outcome study



http://nuffieldbioethics.org/wp-content/uploads/2014/06/TMS.jpg;
http://www.prescouter.com/2012/09/transcranial-magnetic-stimulation-possible-cure-for-tinnitus/

Non-invasive Neurological Methods

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Cochrane Review (Meng, et al., 2009):

Transcranial magnetic stimulation for tinnitus

Data search retrieved 283 articles. Five trials comprising 233 tinnitus patients, inclusion criteria & included in the review.

MAIN FINDINGS:

- Of the 5 studies included, 3 applied low-frequency rTMS
- Of those 3, only 1 study revealed 'partial improvement' in tinnitus severity & disability
- This improvement was not replicated in two other studies that applied rTMS at the same, low-frequency
- Considering all 5 studies, it was impossible to show an improvement in tinnitus loudness in patients undergoing rTMS
- rTMS is a safe treatment for patients with tinnitus in the short-term, however no data were available to verify safety in the long-term.

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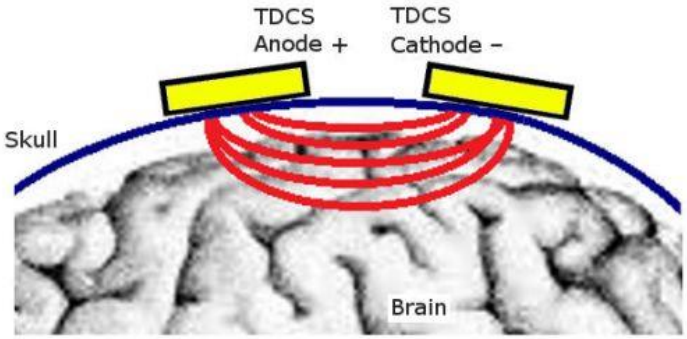
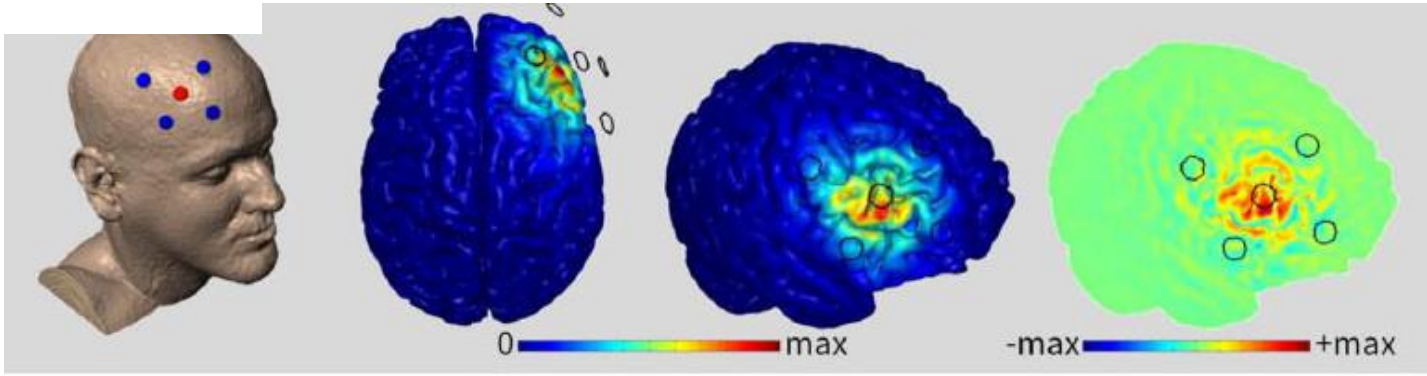
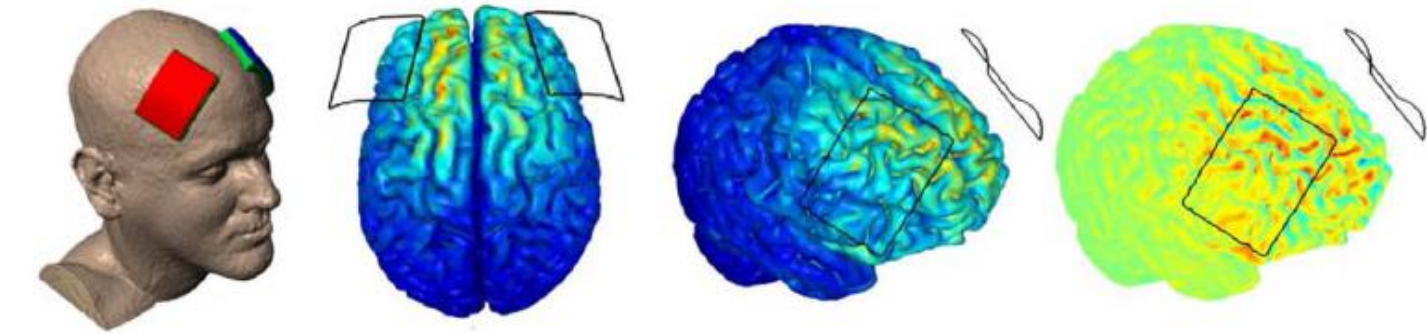


- **Transcranial direct current stimulation (tDCS)**
- **High-definition, transcranial direct current stimulation (HD-tDCS)**





Non-invasive Neurological Methods

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(Shekhawat, et al., 2015)
HD-tDCS (*n* = 27)

- HD-tDCS has not (yet) been used extensively in tinnitus research
- The conventional large sponges are replaced with smaller gel electrodes
- 4 electrodes encourage current flow limited to areas below the placement sites (more focal)
- Present research looking at parameters most effective at inducing tinnitus relief
- **RESULTS:** Left temporoparietal & DLPFC placements equally effective at reducing tinnitus loudness & annoyance

"Does provide a change in excitability in underlying cortical activity, but for tDCS & rTMS, it does not last"
(Searchfield, 2015)

Polymorphism & plasticity

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- BDNF – Brain-derived neurotrophic factor
- Protein, in humans, encoded by the BDNF gene. BDNF is a part of the neurotrophin group of growth factors
- Neurotrophic factors are located in the brain & the periphery
- Like “Miracle Grow” for the brain
- But, there can be polymorphism in genes related to plasticity
- BDNF polymorphism is associated with abnormal reaction to training (e.g., rTMS – some will not show the same response & vary as a function of genotype)
- **Know the patient or participant genotype or ability to metabolise, before medication, treatment or training…**

(Kleim, 2015)

Psychological and Counselling Therapies

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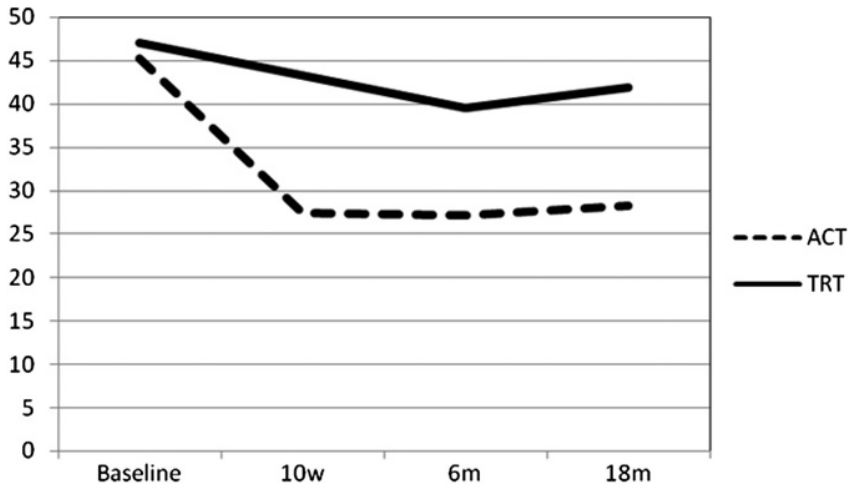
(Westin, et al., 2011)

Acceptance and Commitment Therapy versus Tinnitus Retraining Therapy in the treatment of tinnitus: A randomised controlled trial

- (*n* = 64) Participants with normal hearing & tinnitus, randomised to ACT, TRT, or wait-list control (WLC) groups
- ACT required 10 weekly 60 min sessions
- TRT required one 150 min session, one 30 min follow-up & continued daily use of wearable sound generators for a recommended period of at least 8 h/day for 18 months
- Assessments were made at baseline, 10 weeks, 6 months & 18 months.



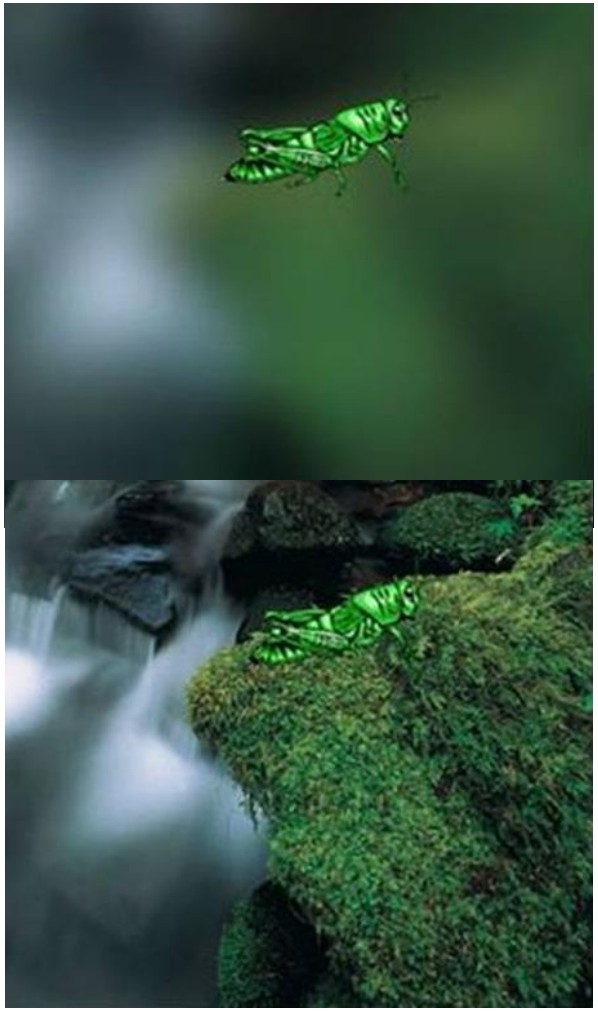
Tinnitus Handicap Inventory (THI) average scores during the study period

Sound ‘therapy’

Used in conjunction with other strategies (directly or indirectly)

- Includes the use of:
  - Background sound (lowest level that provides the greatest subjective benefit)
  - Hearing aids
  - Total or partial masking (relief, control)
  - Music therapy

- Plays a role in:
  - Reducing the attention drawn to the tinnitus
  - Reducing subjective loudness of the tinnitus
  - Substituting a less disruptive noise (background sound) for an unpleasant one (tinnitus)
  - Provides a shift in locus of control (back to patient/client)



Sound Provision (Audiological)

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Self-assessed hearing abilities in middle- and older-age adults: A stratified sampling approach

- (*n* = 200) Per survey "Difficulty with hearing?" (YES/NO) and subjective impression (HIGH/LOW) abilities per the Speech, Spatial & Qualities questionnaire

- People in the YES (hearing difficulty) but HIGH (abilities) groups also scored significantly higher on a question about tinnitus incidence, suggesting that "hearing difficulty" extends to audibility of unwanted, internally-generated noises

Does treating "hearing difficulty" with hearing aids help with tinnitus?

(Nobel, et al., 2012)

Sound Provision (Audiological)

Hearing aids as an adjunct to counseling: Tinnitus patients who choose amplification do better than those that don't

- All received group counselling (n = 58)

AFTER COUNSELLING:

- Received hearing aids (n = 29); significant reduction THQ shifted from 59% to 37% ($p < 0.0001$)
- Opted not to proceed with hearing aids (n = 29); THQ shifted from 51% to 41% (Not Significant)

(Searchfield, Kaur & Martin 2010)

Sound Provision (Audiological)

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Hearing aids and tinnitus therapy: a 25-year experience

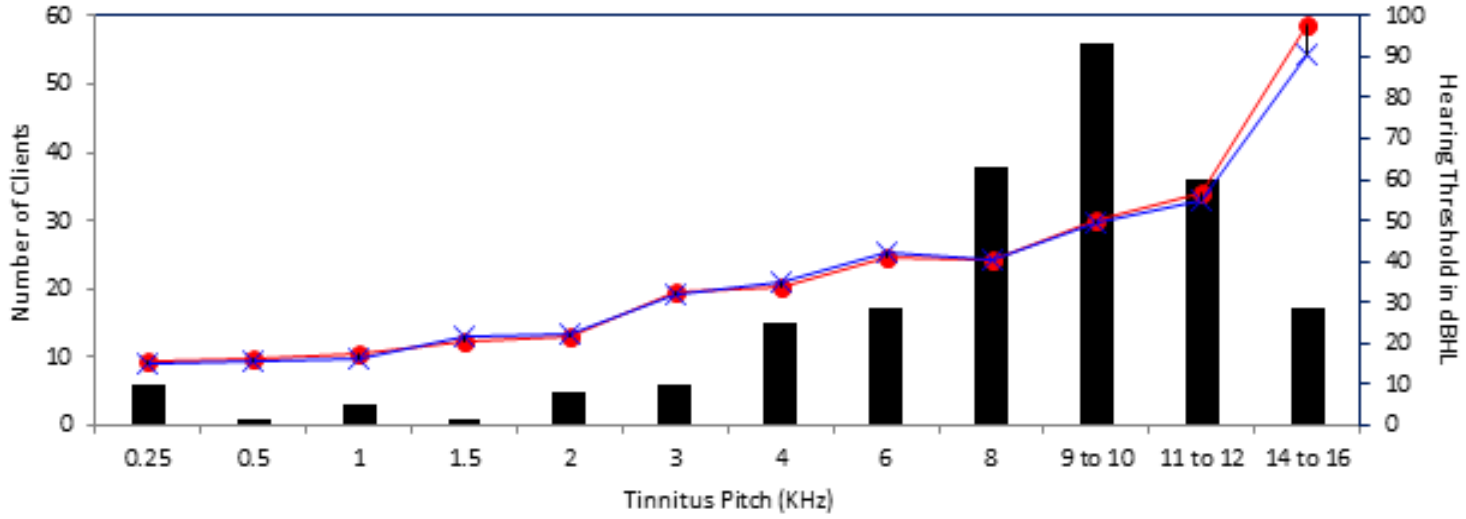
M I Trotter[a1] [c1] and I Donaldson[a1]

- (*n* = 1440) patients fit with 1 or 2 hearing aids depending on clinical presentation & amplification needs
- Not an experimental design
- (n = 554; unilaterally aided) or 67% and (n = 424; bilaterally aided) or 69% - reported some improvement in tinnitus after aiding
- Significant improvement in tinnitus, when comparing outcomes following the adoption of digital (versus analogue) hearing aid fitting- unilateral ($p < 0.001$) and bilateral ($p < 0.001$)

Considered the improvement due to broader bandwidth & improved tinnitus masking at higher frequencies

(Trotter & Donaldson, 2008)

Sound Provision (Audiological)



Average, subjective tinnitus pitch-match with right and left hearing thresholds plotted in red and blue respectively (N = 192)

(Shekhawat, Searchfield & Stinear, 2013)

Sound Provision (Audiological)

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2002 – Present: University of Auckland Hearing & Tinnitus Clinic

- Not an experimental design
- Those with hearing loss & tinnitus with more preserved low-frequency hearing generally receive improvement in tinnitus with hearing aids
- Those with poor low-frequency hearing tended to receive little improvement in tinnitus with hearing aids & did better with other strategies (e.g., combination devices)
- Those with high-frequency tinnitus, pitch-matched to a frequency region above/outside the bandwidth provided by device may not perceive as much benefit, due to lack of sufficient tinnitus masking

(Searchfield, 2015)

Sound Provision (Customised)

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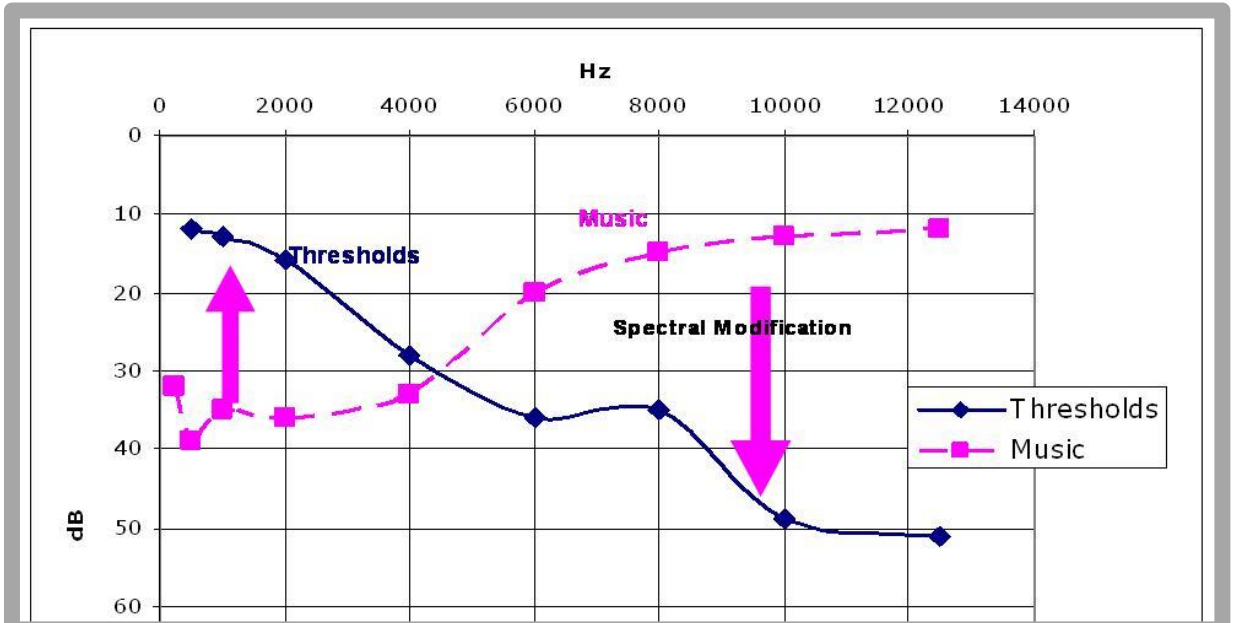
- Neuromonics

- Case or category-dependant, generally designed as a 6-month protocol but may take longer for those not ideal Tier 1 candidates (e.g., Ménière's)
- Desensitization via passive listening with tinnitus embedded in spectrally-modified music (music + BBN in Phase 1 of treatment)
- Music features slow tempo to facilitate relaxation; uses extended bandwidth (12.5 kHz)
- Uses variety of counselling styles addressing 'Patient Expectation' & 'Nurturing' & promotes interactive patient discussion
- Relate case history to individual tinnitus experience, supply equipment training, determine goals, manage expectations, provision of tinnitus information/self-help & hand-outs
- Requires clinician(s) to undergo training to deliver the technique



An Independent Review of Neuromonics Tinnitus Treatment Controlled Clinical Trials

JAMES A. HENRY[1,2] AND JOE ISTVAN[1]

[1] VA RR&D National Center for Rehabilitative Auditory Research, VA Medical Center, Oregon, United States of America

[2] Department of Otolaryngology/Head and Neck Surgery, Oregon Health & Science University (OHSU), United States of America

- Reviewed 3, published controlled clinical trials of Neuromonics (1996, 2002b, 2007)
- Used the Consolidated Standards of Reporting Trials (CONSORT) as the framework – providing a rigorous review criteria for randomised clinical trials
- Cited a lack of methodological transparency, & the proprietary nature of Neuromonics as limitations with regards to evaluating the merit of Neuromonics

Clinical Studies

(Provided by Paul Davis, 15TH July 2015)

#	Study	n	Description	Location	Succ
1	T1 – Feasibility	30	Neuromonics, Single Arm	AUS	N/
2	T2 – NTT vs. SOC (Ear, Nose & Throat Journal 2008)	50	Neuromonics, TRT vs. counseling alone (RCT)	AUS	86%
3	T3 – 1 vs. 2 Phase (Ear & Hearing 2007)	35	Neuromonics, Dose Study (RCT)	AUS	90%
4	Private Practice (Annals of Otol, Rhin, & Laryng 2008)	470	Neuromonics, Multiple Tiers of patients	AUS	92%
5	Lions Ear Institute (2008)	29	Independent, Single Arm	AUS	75%
6	Johnston (Oregon) (2008)	24	Independent, Single Arm	US	72%
7	Tavora-Vieira et al (Internat. Journal of Audiology 2011)	26	Independent, Single Arm, non-std high-hearing loss subjects	AUS	84.6
8	Vieria et al (International Tinnitus Journal 2011)	70	Independent, Single Arm, registry	US/AUS	76%
9	Wazen et al (Otology & Neuro-Otology 2011)	51	Independent, Single Arm	US	81%
10	Hollywood VA (2009)	35	Independent, Single Arm	US / VA	96%
12	AUS Veterans	57	Independent & Neuromonics, Single Arm, patients who failed prev. Tx	AUS /DVA	74%
11	DoD Study (Ft. Rucker)	140	Independent, NTT vs. iPod/ TRT counseling	US / DoD	
13	NAL/Macquarie University	?	Independent, pre/post MEG	AUS	
14	Haven/Oasis II	?	Private Practice/ VA/ DVA	USA/AUS	
	TOTAL	1017		AVG	83%

Self-help and Pervasive Healthcare Approaches

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Pervasive Healthcare

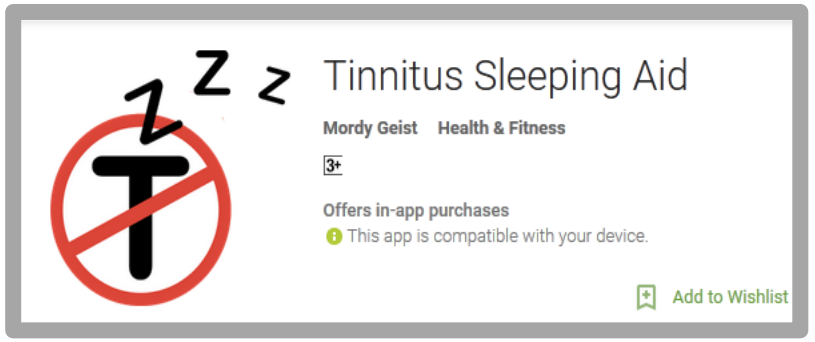
Paving the Way for a Pervasive, User-centered and Preventive Healthcare Model

B. Arnrich[1]; O. Mayora[2]; J. Bardram[3]; G. Tröster[1]

Pervasive Healthcare as a Scientific Discipline

J. E. Bardram

IT University of Copenhagen, Copenhagen, Denmark



(Arnrich, et al., 2010; Bardram, 2008)

Neuroplasticity & Training Models

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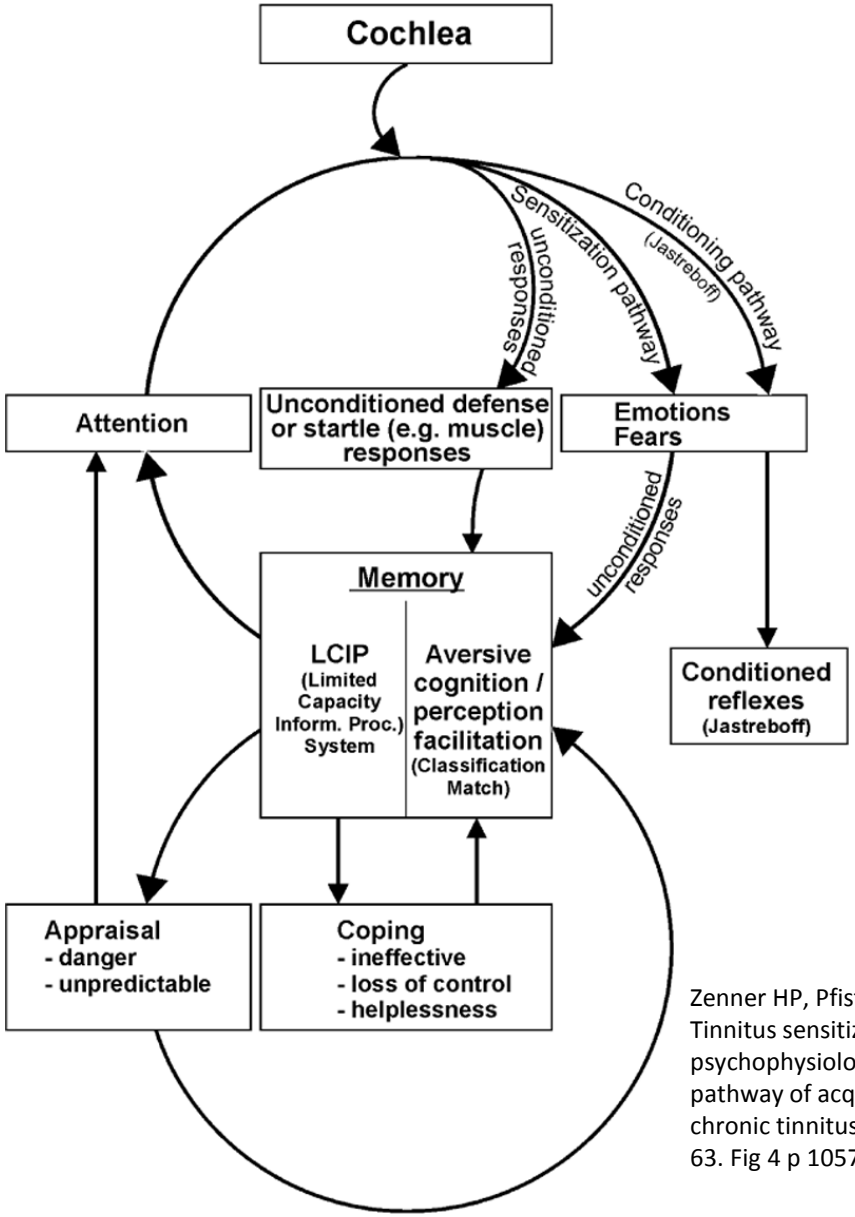
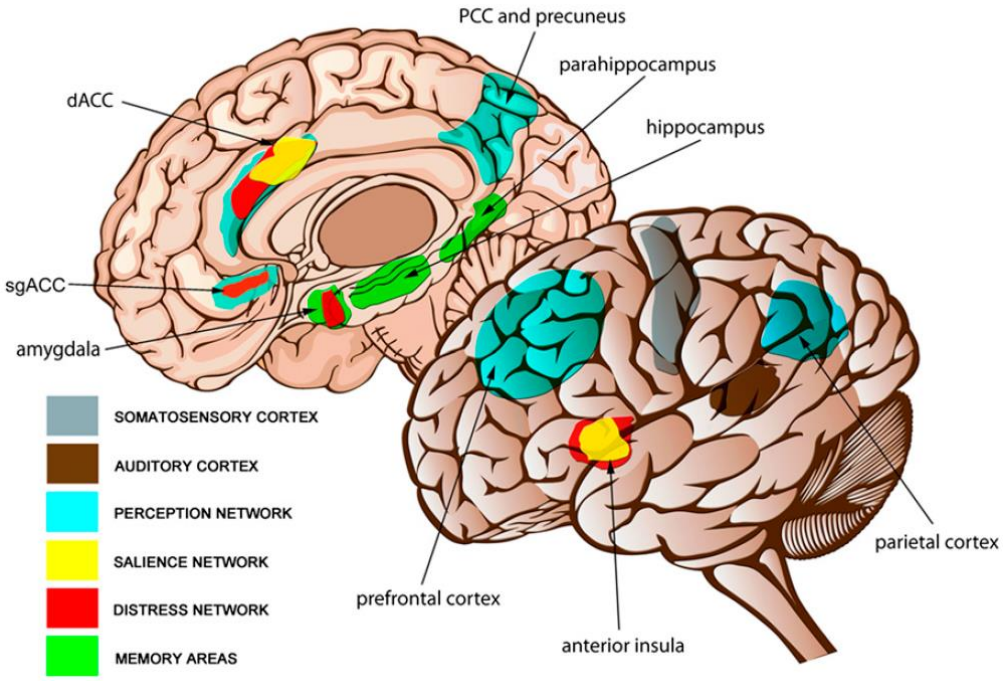
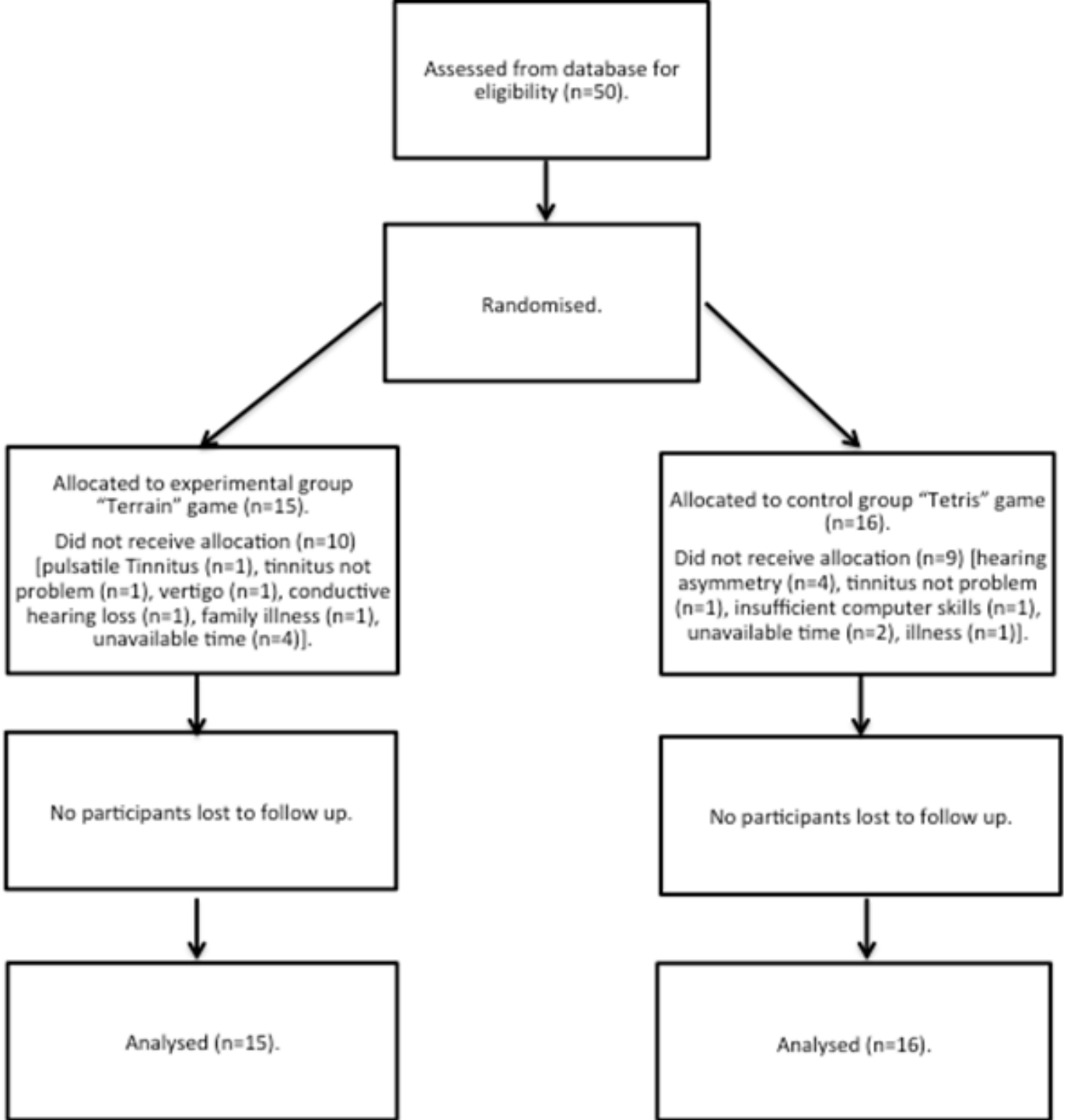
- Cascade
- Reorganisation
- Spontaneous
- Synchronous
- Resultant “mimicry”
- Sound template mismatch
- Perceptually stands out
- Non-auditory factors





Zenner HP, Pfister M, Birbaumer N.(2006) Tinnitus sensitization: Sensory and psychophysiological aspects of a new pathway of acquired centralization of chronic tinnitus. *Otol Neurotol*. 27(8):1054-63. Fig 4 p 1057

De Ridder, D., A. B. Elgoyhen, et al. (2011). Phantom percepts: Tinnitus and pain as persisting aversive memory networks. *Proceedings of the National Academy of Science of the United States of America* [Early Edition]: 1-6.

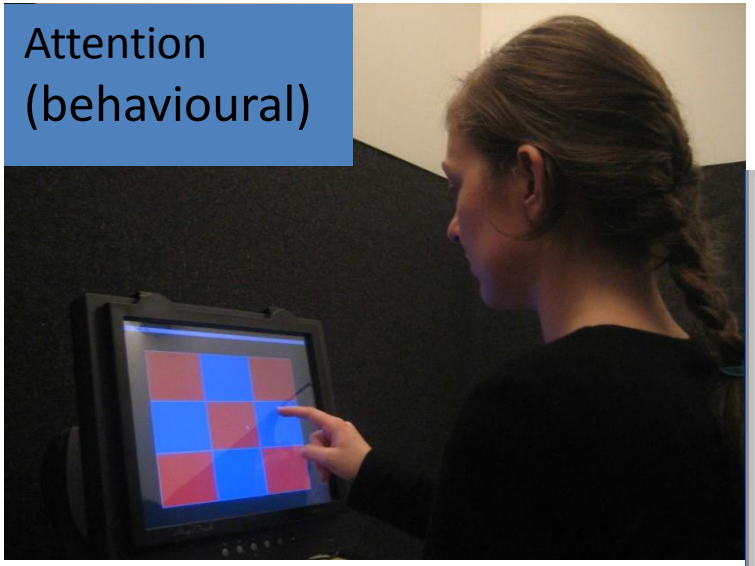

Assessed from database for eligibility (n=50).
Randomised.
Allocated to experimental group "Terrain" game (n=15).
Did not receive allocation (n=10) [pulsatile Tinnitus (n=1), tinnitus not problem (n=1), vertigo (n=1), conductive hearing loss (n=1), family illness (n=1), unavailable time (n=4)].
Allocated to control group "Tetris" game (n=16).
Did not receive allocation (n=9) [hearing asymmetry (n=4), tinnitus not problem (n=1), insufficient computer skills (n=1), unavailable time (n=2), illness (n=1)].
No participants lost to follow up.
No participants lost to follow up.
Analysed (n=15).
Analysed (n=16).

p<0.05 = * p<0.01 = **	Training group (Terrain, n=15)	Control group (Tetris, n=16)
Demographics		
Age	52.3 (10.6)	62.3 (4.6)
Gender	3 Female, 12 Male	7 Female, 9 Male
Questionnaires		
TFI	30.7 (17.1)	25.6 (17.1)
THI	25.5 (16.0)	18.6 (10.9)
Rating scales		
Problem	2.7 (0.7)	2.6 (0.7)
Loudness	4.8 (1.9)	5.1 (2.3)
Uncomfortable	4.9 (2.3)	5.3 (2.3)
Annoying	4.9 (1.8)	5.1 (2.7)
Ignore	6.1 (2.7)	4.9 (2.6)
Unpleasant	5.2 (1.6)	5.1 (2.4)

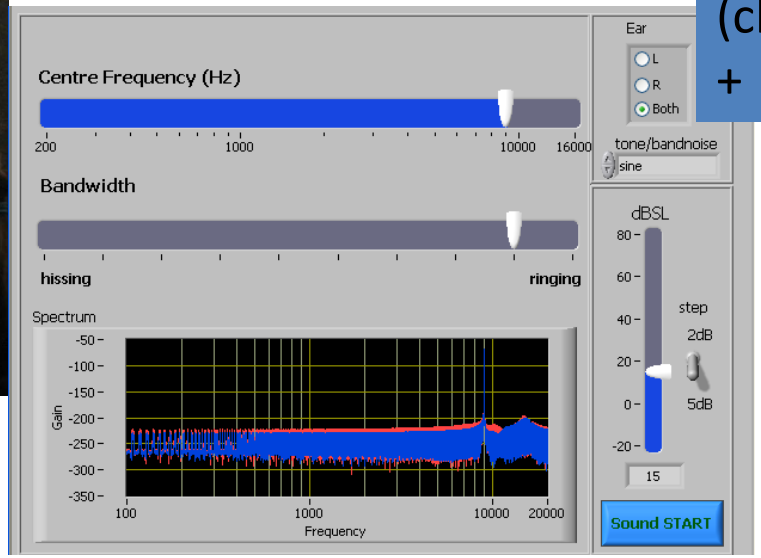
p<0.05 = * p<0.01 = **	Training group (Terrain, n=15)	Control group (Tetris, n=16)
Psychoacoustic measures		
Pitch kHz	7.8 (3.3)	7.5 (3.0)
MML Right	9.7 (8.0)	5.5 (6.5)
MML Left	8.5 (8.2)	7.3 (7.3)
DASS		
Depression	6.1 (6.0)*	1.9 (3.7)
Anxiety	3.1 (3.3)	3.4 (4.3)
Stress	10.1 (6.77)	6.1 (6.7)
MMSE	29.8 (0.4)	29.5 (0.6)

p<0.05 = * p<0.01 = **	Training group (Terrain, n=15)	Control group (Tetris, n=16)
CSFA		
Deal with problem style	56.8 (16.3)	68.4 (12.8)
Non-coping style	44.9 (14.1)	45.75 (13.6)
Optimism style	44.3 (21.4)	63.5 (12.9)**
Sharing style	56.7 (29.2)	37.6 (22.0)
SSQ		
Speech Hearing	103.8 (23.17)*	80.81 (36.5)
Spatial Rating	141.4 (22.01)	127.9 (31.7)
Sound qualities	141.2 (41.2)	139.8 (33.8)

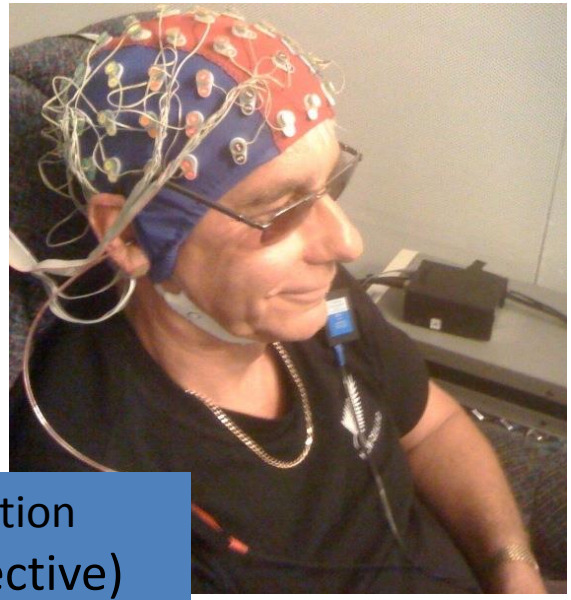
Attention (behavioural)



Tinnitus (characterisation + customisation)

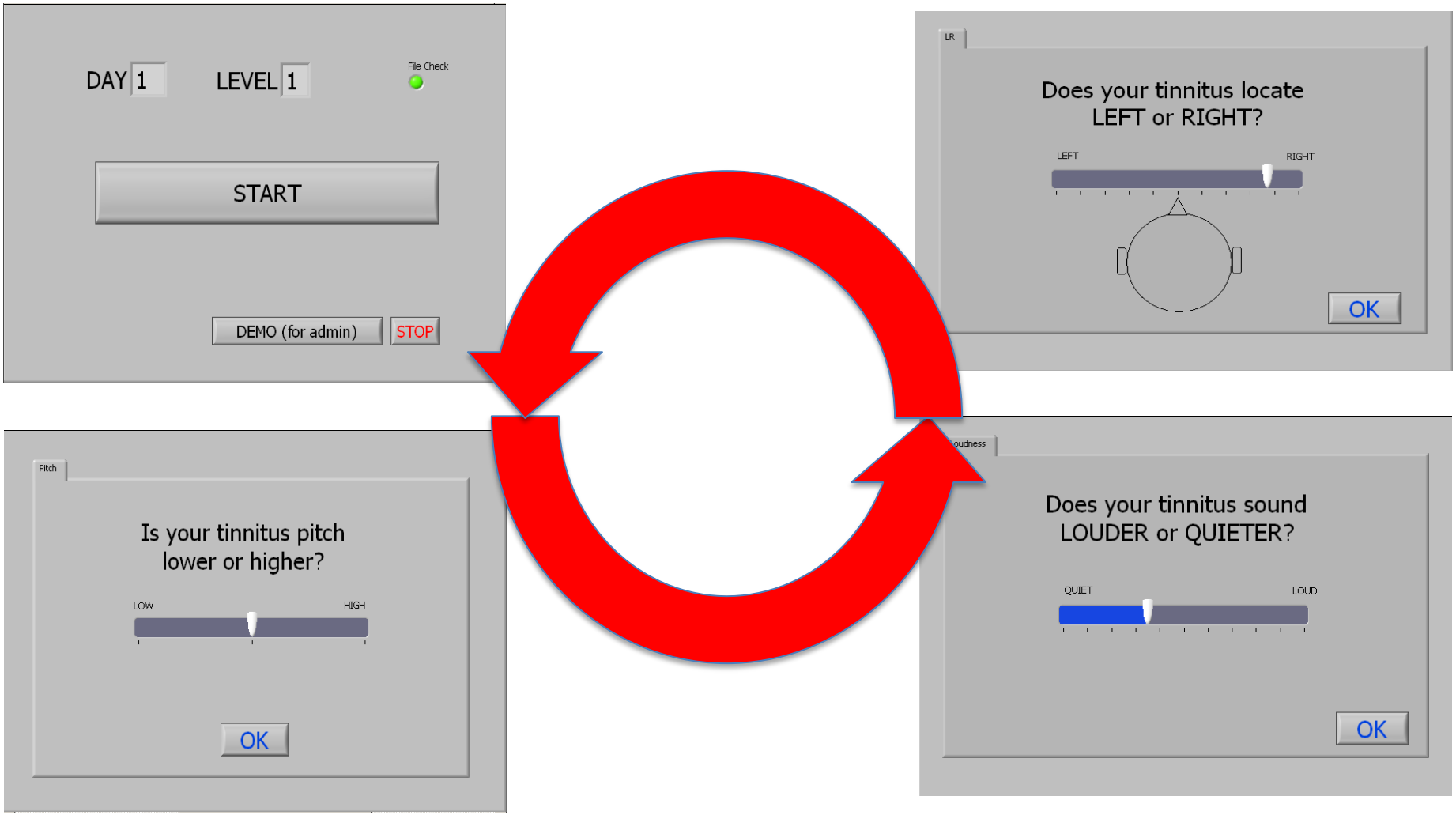


Attention (objective)

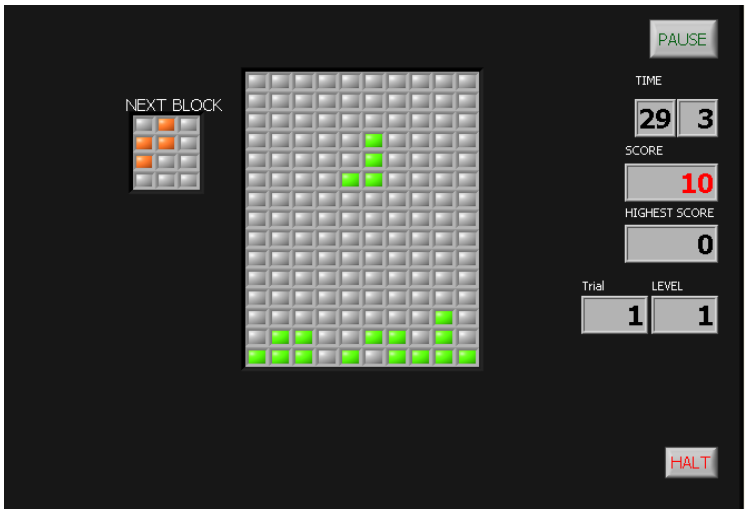


- Capitalise on cortical plasticity
- Un-do negative forms of plasticity to de-emphasize tinnitus
- Engage attentional centres to reduce tinnitus focus (selective attention)
- Pervasive Healthcare

Game – Calibration phase

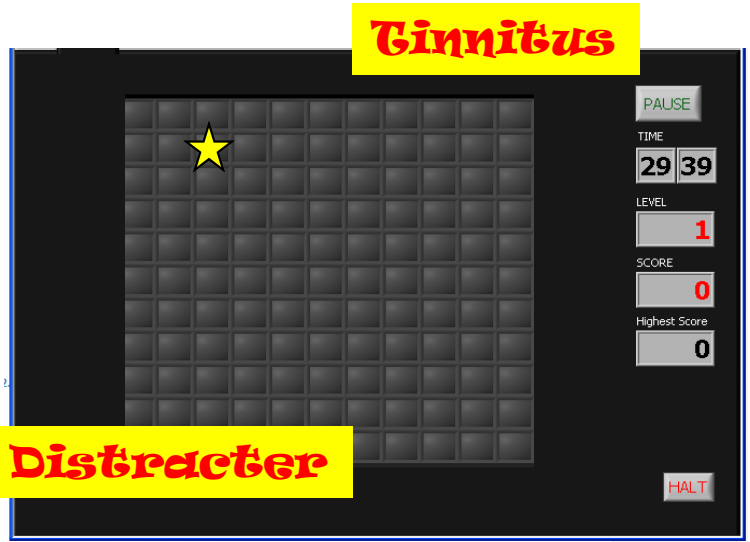


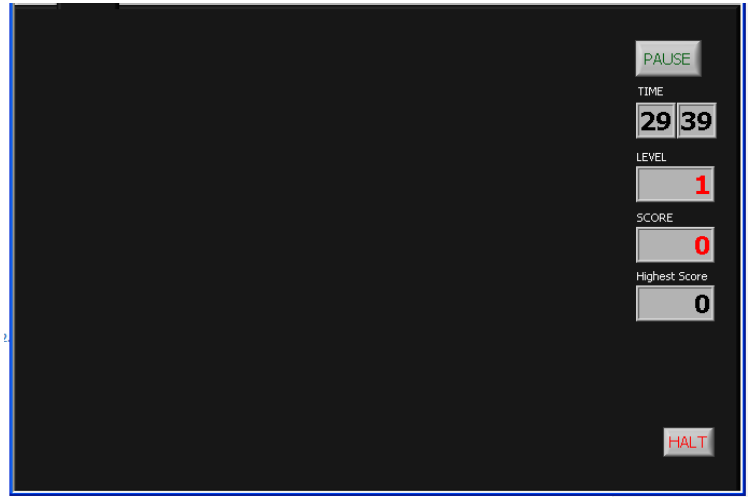
Tetris (N = 16), Control

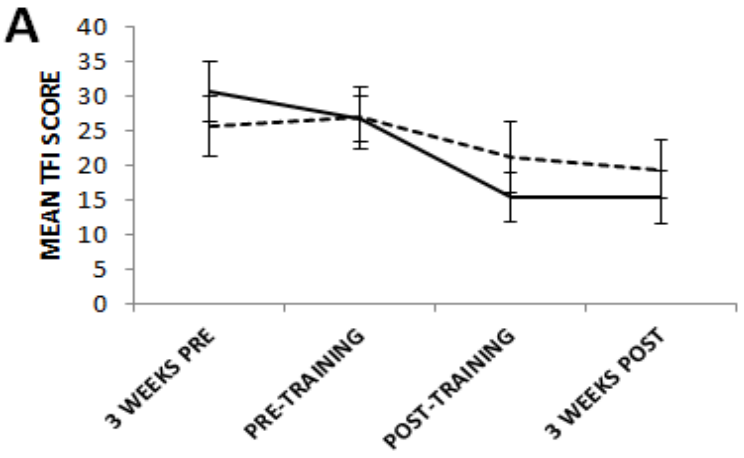


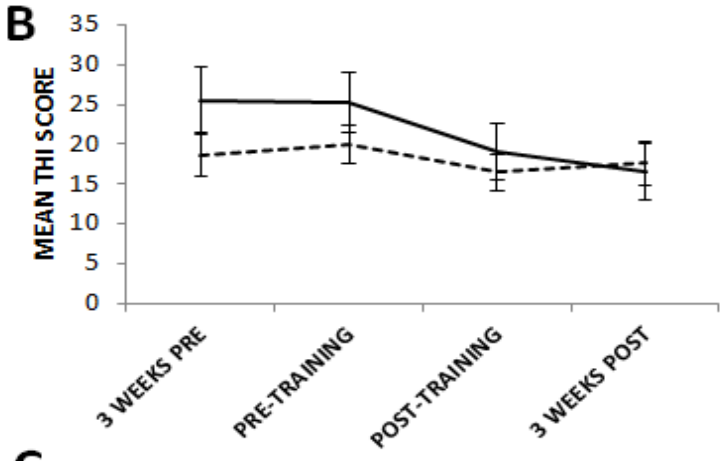
Terrain (N = 15), Experiment

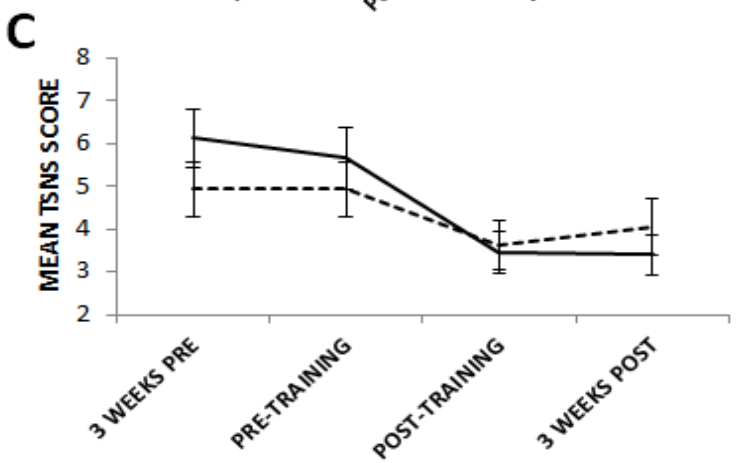
Selective Auditory Attention & Perceptual training











Mean reductions over time:

(A) Tinnitus Functional Index (TFI); ($p<0.01$)

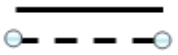
(B) Tinnitus Handicap Inventory (THI); ($p<0.01$)

(C) Tinnitus Severity Numeric Scale (TSNS); ($p<0.01$)
TSNS-Ignore scale

Terrain: TFI was correlated with a reduction in N1 latency in the 630 Hz attend condition ($r=0.55$, $p<0.05$)

Tetris: No similar correlations found

Terrain (experimental)
Tetris (control)



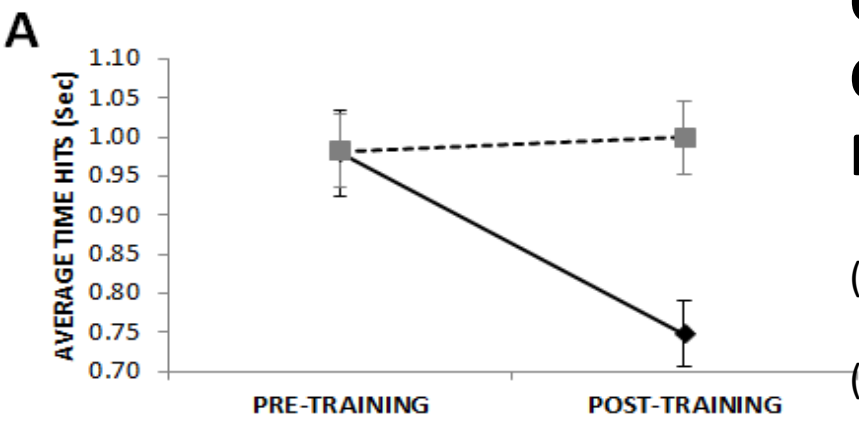
Error bars represent standard error of the mean

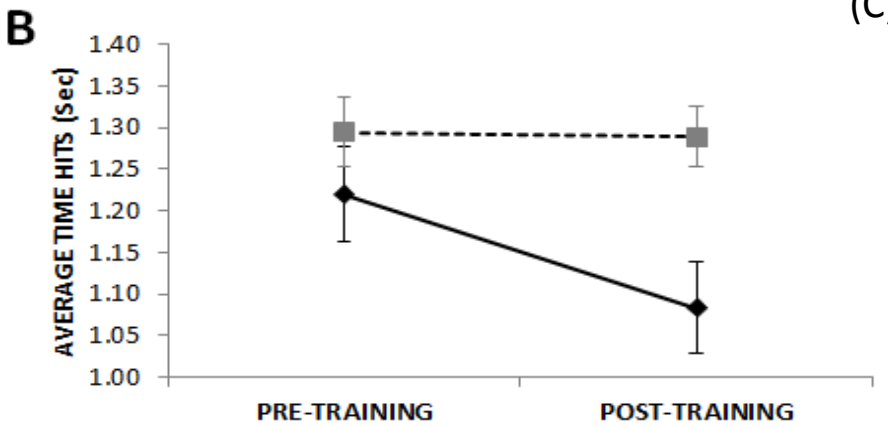
Change in average time hits for the Comprehensive Attention Battery ® Mean reductions over time:

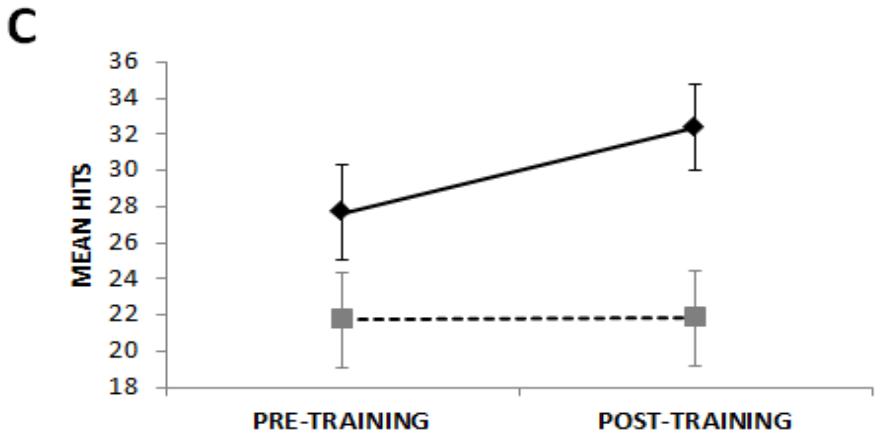
(A) AVMTv2 – faster visual-only task; ($p<0.001$)

(B) AVMTm2 – faster mixed auditory & visual task; ($p<0.005$)

(C) AVMTm2 – change in mean hits; ($p=0.035$)



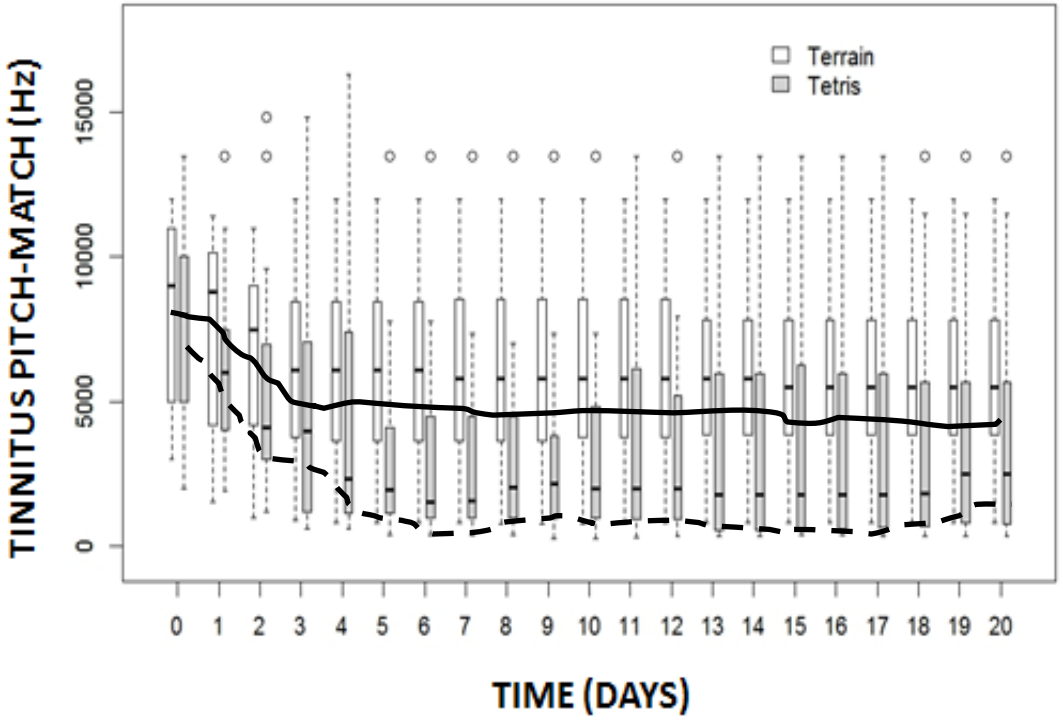




- Terrain: faster & more accurate post-training
- When percentage of improvement that could be due to a learning effect was factored out...

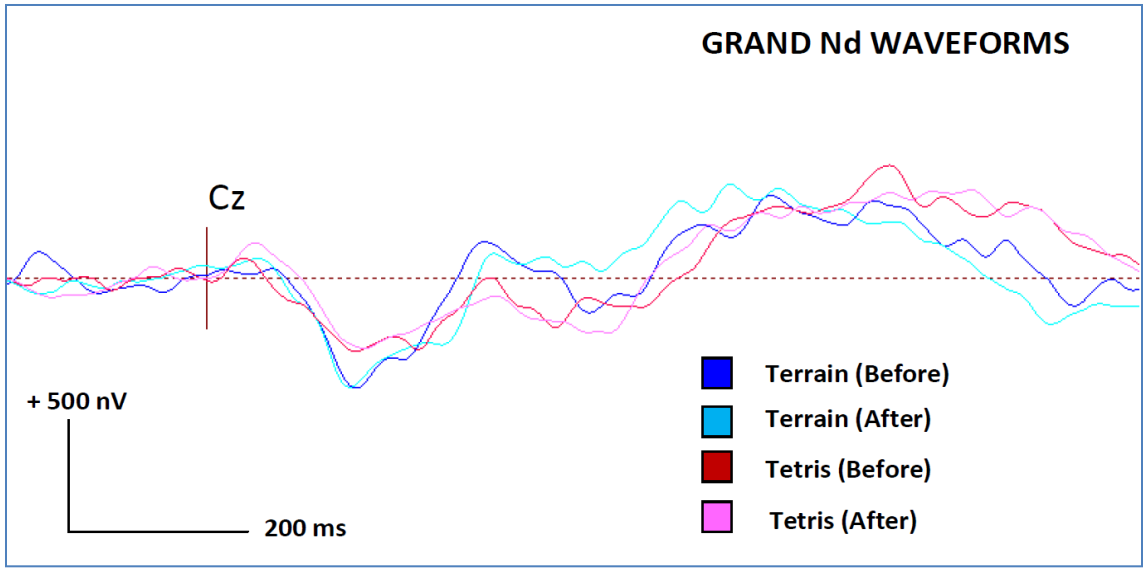
Terrain (experimental)
Tetris (control)

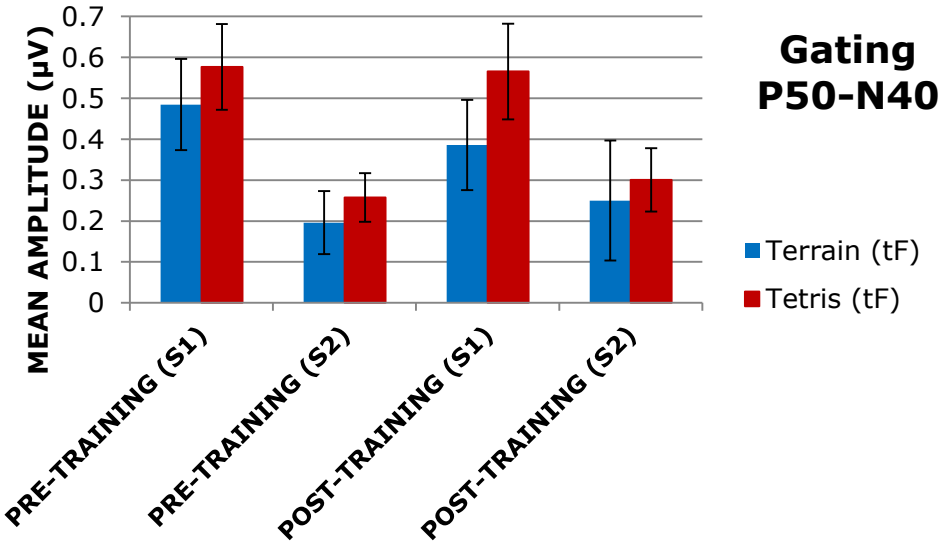
Error bars represent standard error of the mean



Daily Tinnitus Calibration – observed shifts in tinnitus pitch (days 3→5):

- Octave confusion – between tinnitus percept & potential matching tone presented 1 octave removed from tinnitus pitch
- Familiarisation – Drop in tinnitus pitch, both training groups; more reliable indicator of tinnitus characterisation?
- Implication for interpretation – stability of current single-session pitch matching and its use after, as an indication or mechanism of effect; treatment focus
- Implication for animal-based models – require behavioural responses to tinnitus-matched sounds for identification of tinnitus presence





Gating P50-N40

Conclusions

- Training effects may be due to improvement in: selective attention, overall supervisory or executive attention control (or perhaps, both)
- Attention found to significantly improve with training, for tasks with greater cognitive load - faster target presentation.
- Terrain participants had significantly better attention-related outcomes than Tetris – may be due to the type of attention primarily trained (selective) or due to training domain (auditory)
- Whether due to selective attention, the auditory domain or both, those that engaged in Terrain had a significantly greater reduction in TFI and the THI than Tetris

Conclusions

- Both games were reported as positive & enjoyable by participants consistent with calls for practical incentive-based training, capitalising on top-down functions such as intellect & personal drive

> Thanks
> Completed the first game and got to level 3. Scored 23 points.
> Will persevere daily.

> I couldn't fit all this into the space in the log book! And you can see what I've been thinking about when playing the game as I wait for the next target sound to be played.

> **Score of 47**, wow I am really amazed!
>
> I have got the hang of it now and I did not get stuck once. There were a few times when I had to move around to work out which way to go. It helps to listen and see if you can detect small changes. This reduces the risk of straying too far "off course".

- Format is consistent with a pervasive healthcare model

Conclusions

- N1 has been associated with enhancement due to attention, but here it does not appear to reflect or appear enhanced by, training-related change

- Jacobson et al. (1996) found tinnitus participant's demonstrated longer N1 latencies compared to normal controls, suggesting this a possible feature for individuals with tinnitus

  – perhaps N1 latency, rather than the amplitude, is more sensitive to this type of training?

- Before & after these training-based paradigms, sensory gating appears normal for those with tinnitus

Conclusions - overall

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Only consider high-level, evidence-based treatments?

Consider the individual; & clinically, medically-relevant effects

- Large scale, controlled research studies featuring an intervention & showing modest benefit are considered high-level evidence…

  …but, such modest/small benefit may be clinically irrelevant for a particular patient

- If an intervention has been shown to halt tinnitus in certain case-series of a specific, rare, sub-form of tinnitus (e.g., carbamazepine treatment in ‘‘type-writer-tinnitus’’), it is considered to be of relative low evidence…

  …but, this treatment has absolute clinical relevance for the affected patient

(Langguth, et al., 2011; p. 432)

Conclusions - overall

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Only consider high-level, evidence-based treatments?

"Case studies can be salient & we can learn much [from them]…

…randomised control trials are not always, the 'gold standard' *for everyone.*"

(Kleim, 2015)

Acknowledgements

- **Research Participants**
- Dr. Grant Searchfield
- Dr. Ron Goodey
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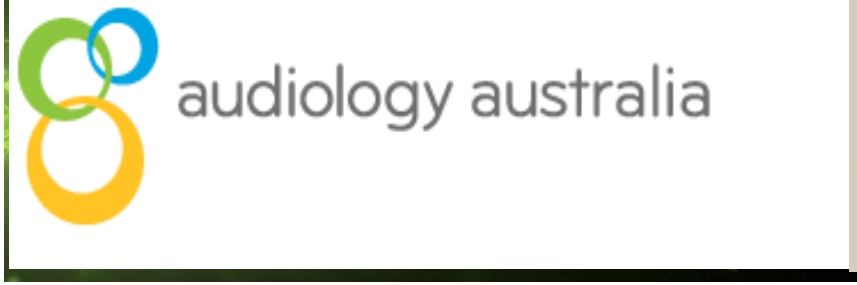
- Dr. David Welch
- Dr. Mike Sanders
- University of Auckland Audiology Section, Research & Clinical Teams
- University of Canterbury, Department of Communication Disorders

Sincere Thanks



- Audiology Australia – Marg
- Audiology Australia members and affiliates
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- Macquarie University
- Australian Hearing Hub

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