Tinnitus Treatment – State of the Art

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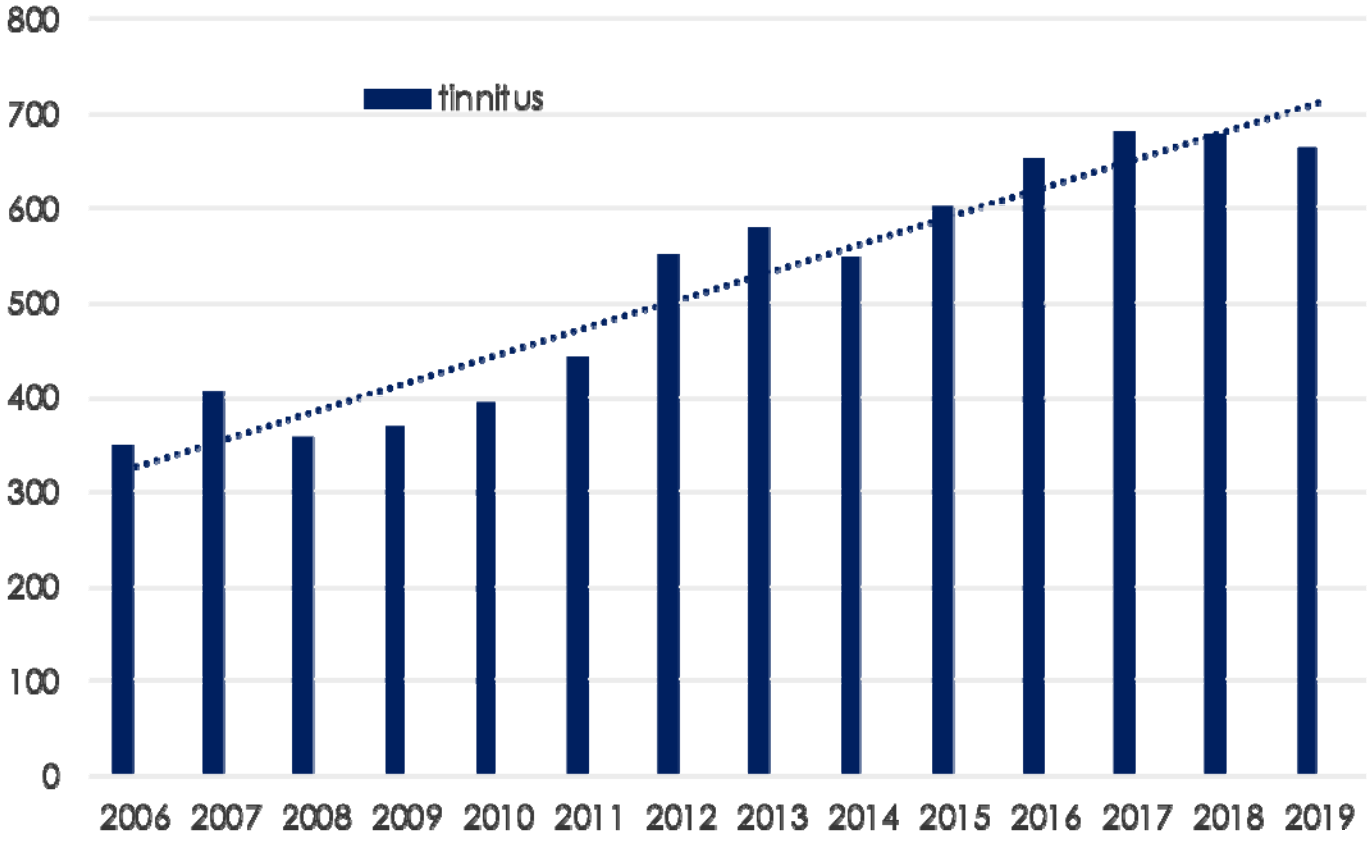
Klinik für Psychiatrie und Psychotherapie der Universität Regensburg
am Bezirksklinikum Regensburg

Was findet sich im Internet ?

Fortschritte in der Tinnitustherapie

Zahl der jährlichen Publikationen in pub med:



Fortschritte in der Tinnitustherapie

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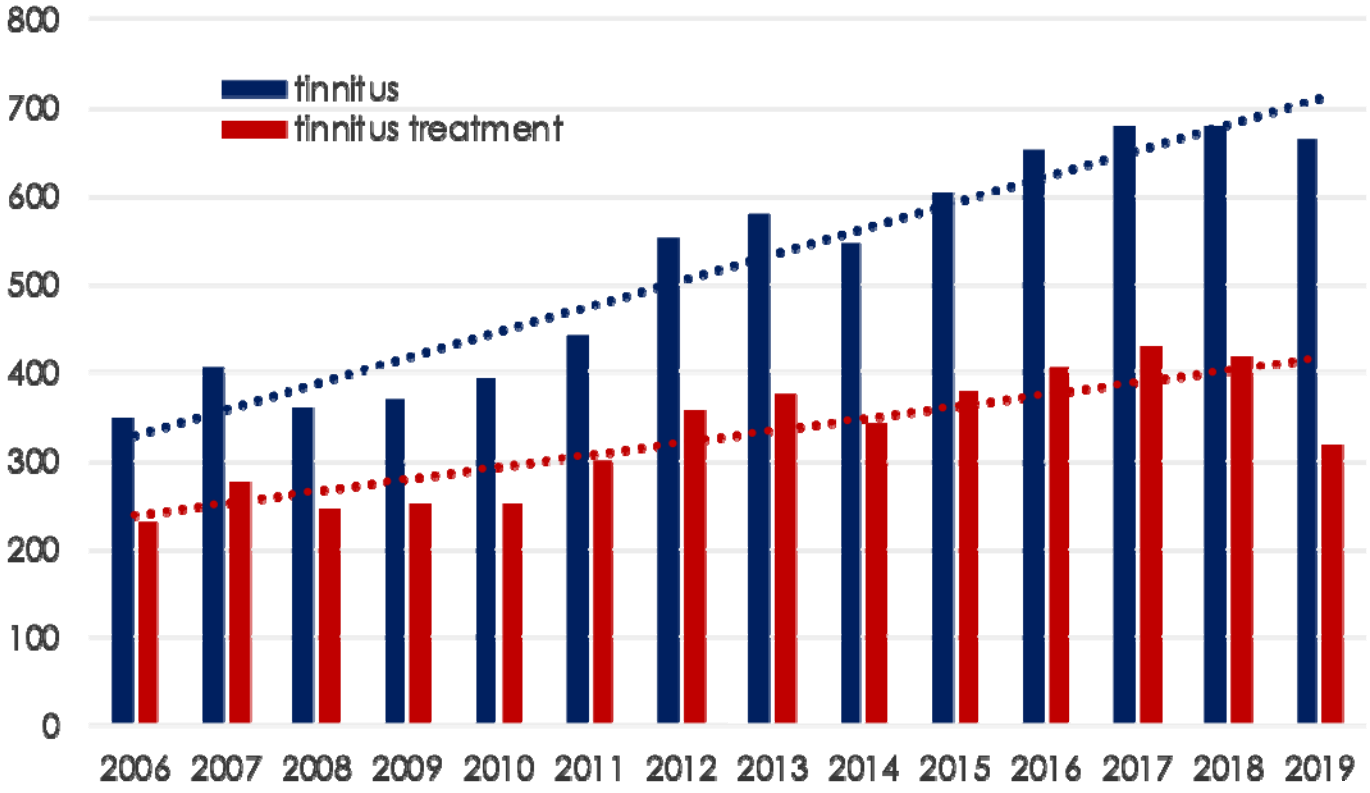
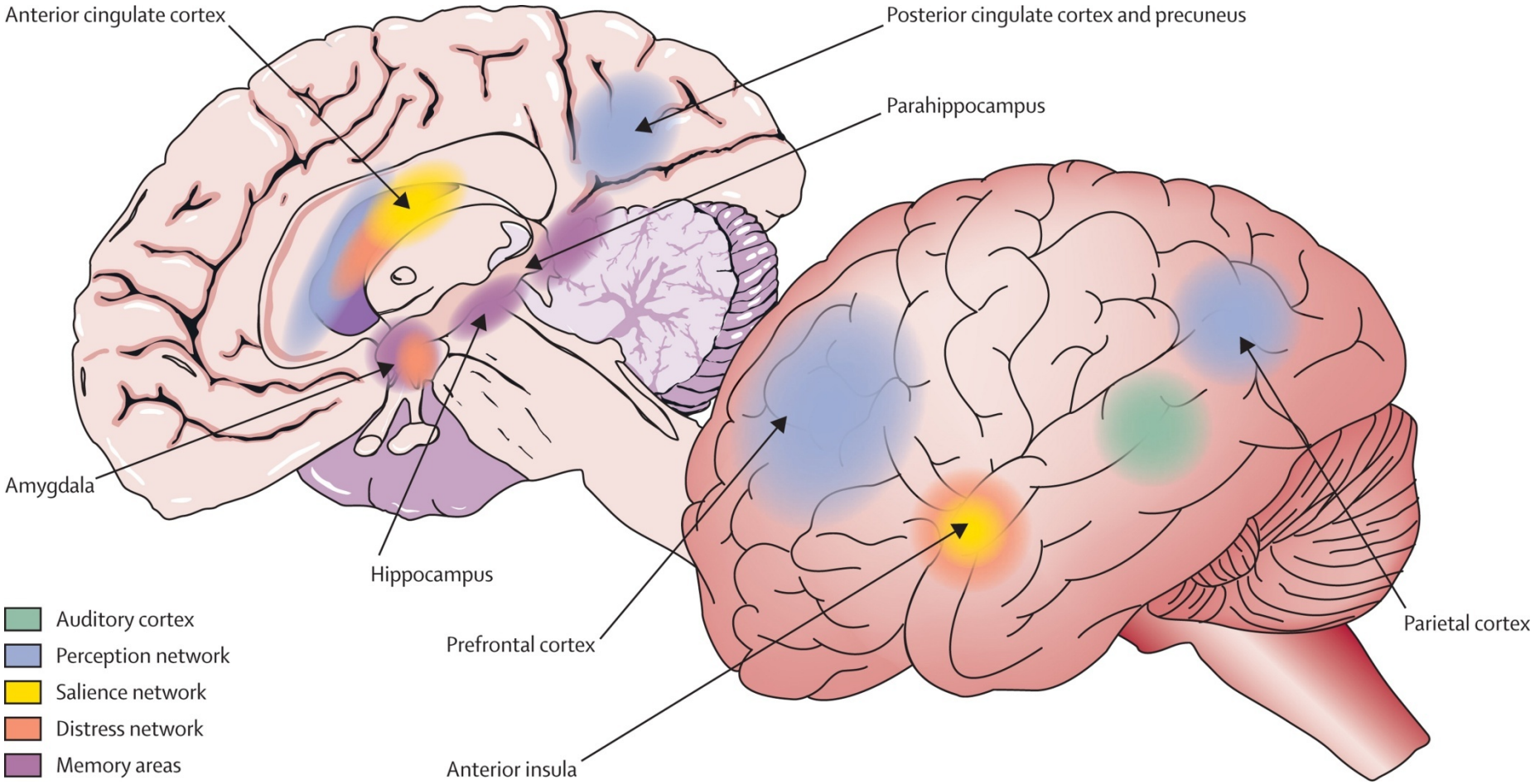
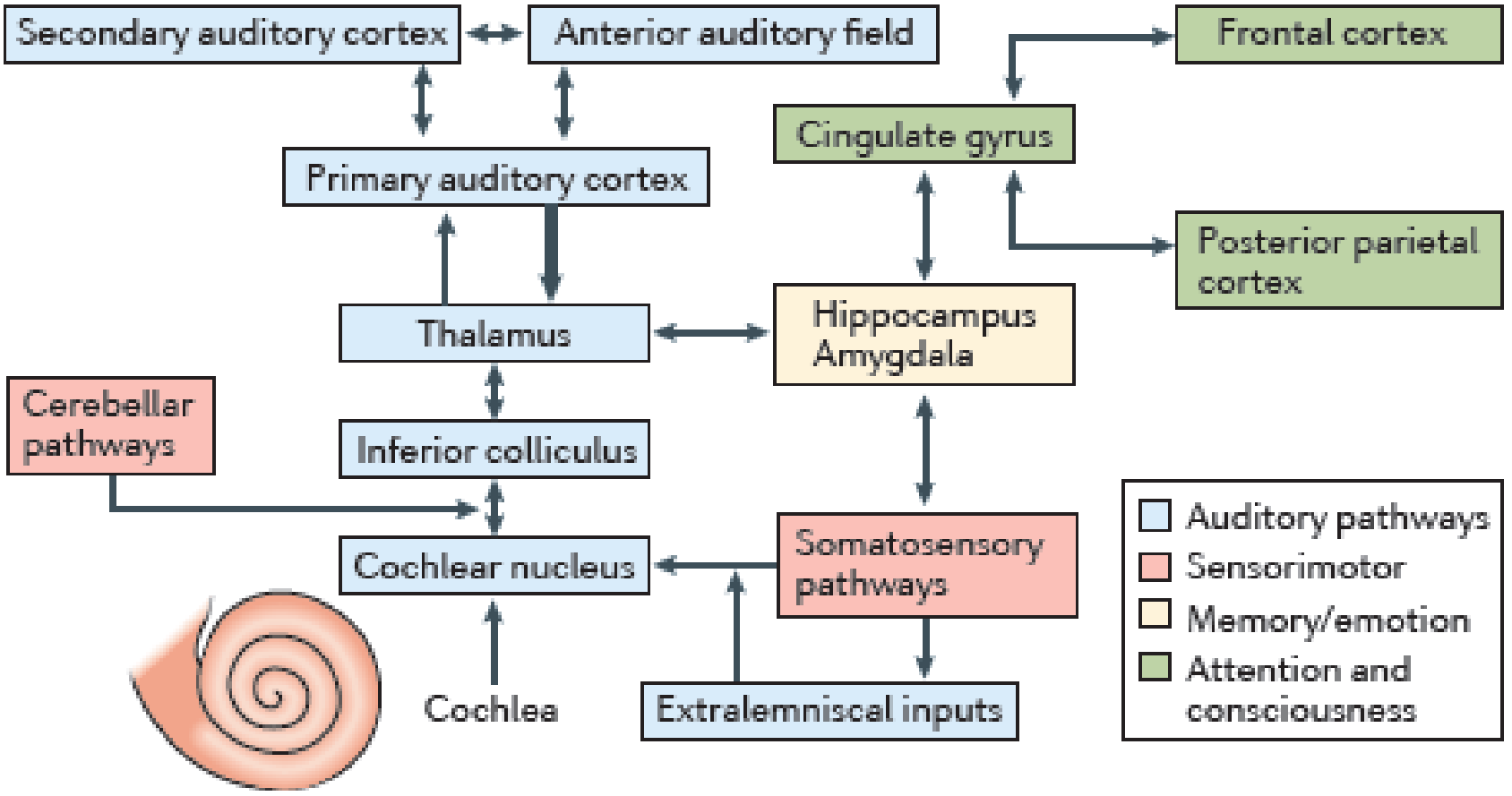


Verständnis der Pathophysiologie



Langguth et al, Lancet Neurology 2013

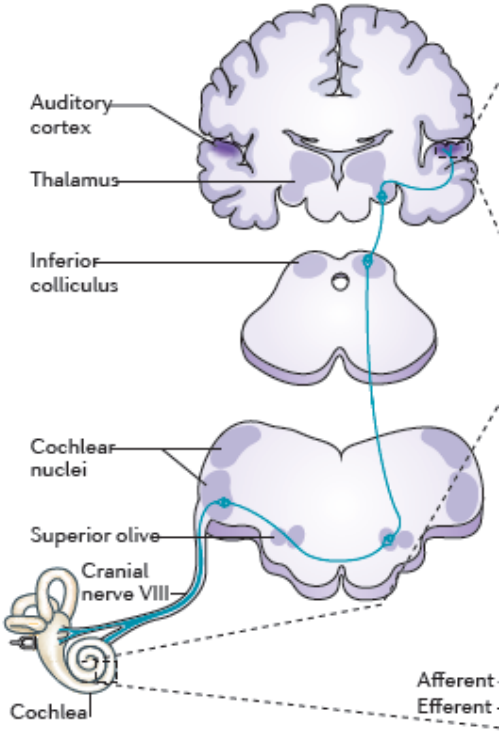
Involvement of many structures beyond the auditory cortex

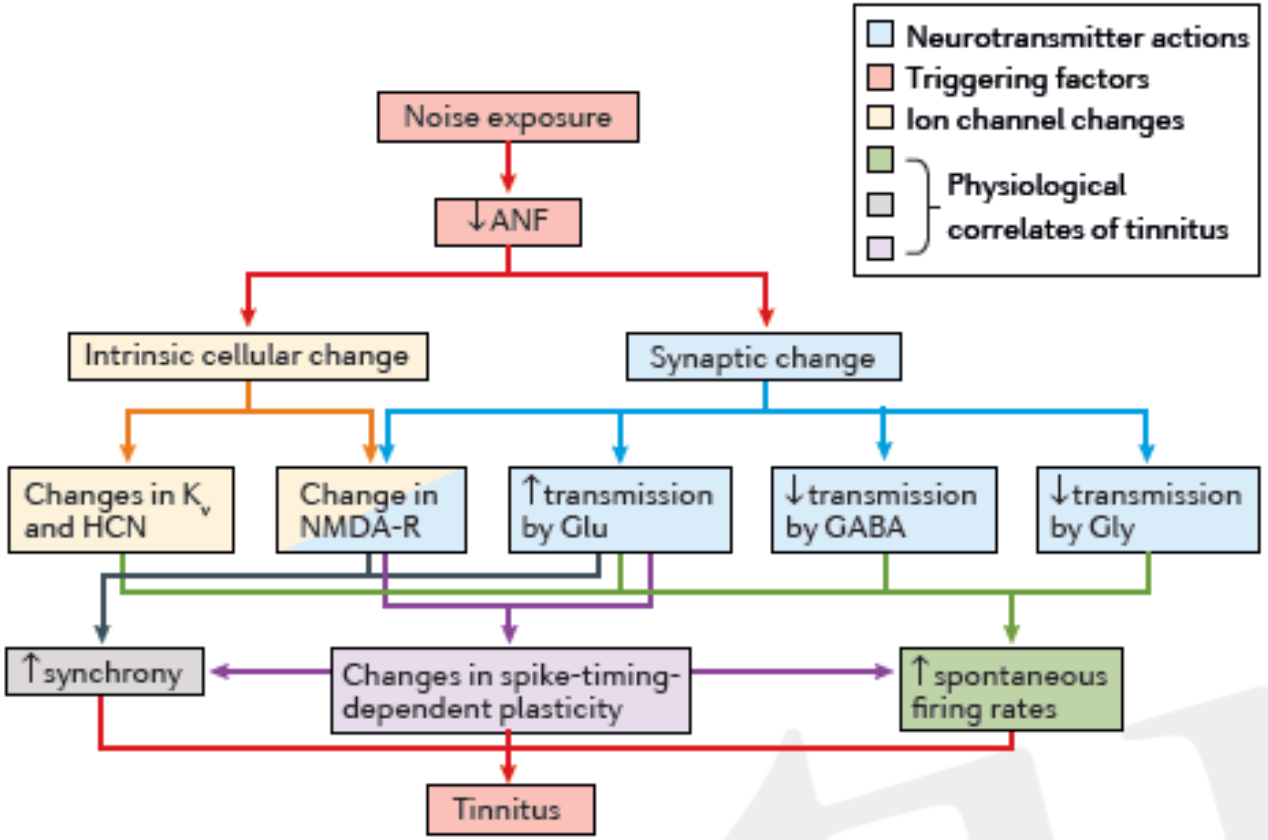


NATURE REVIEWS | NEUROLOGY

Susan E. Shore[1], Larry E. Roberts[2] and Berthold Langguth[3]

Verständnis der Pathophysiologie



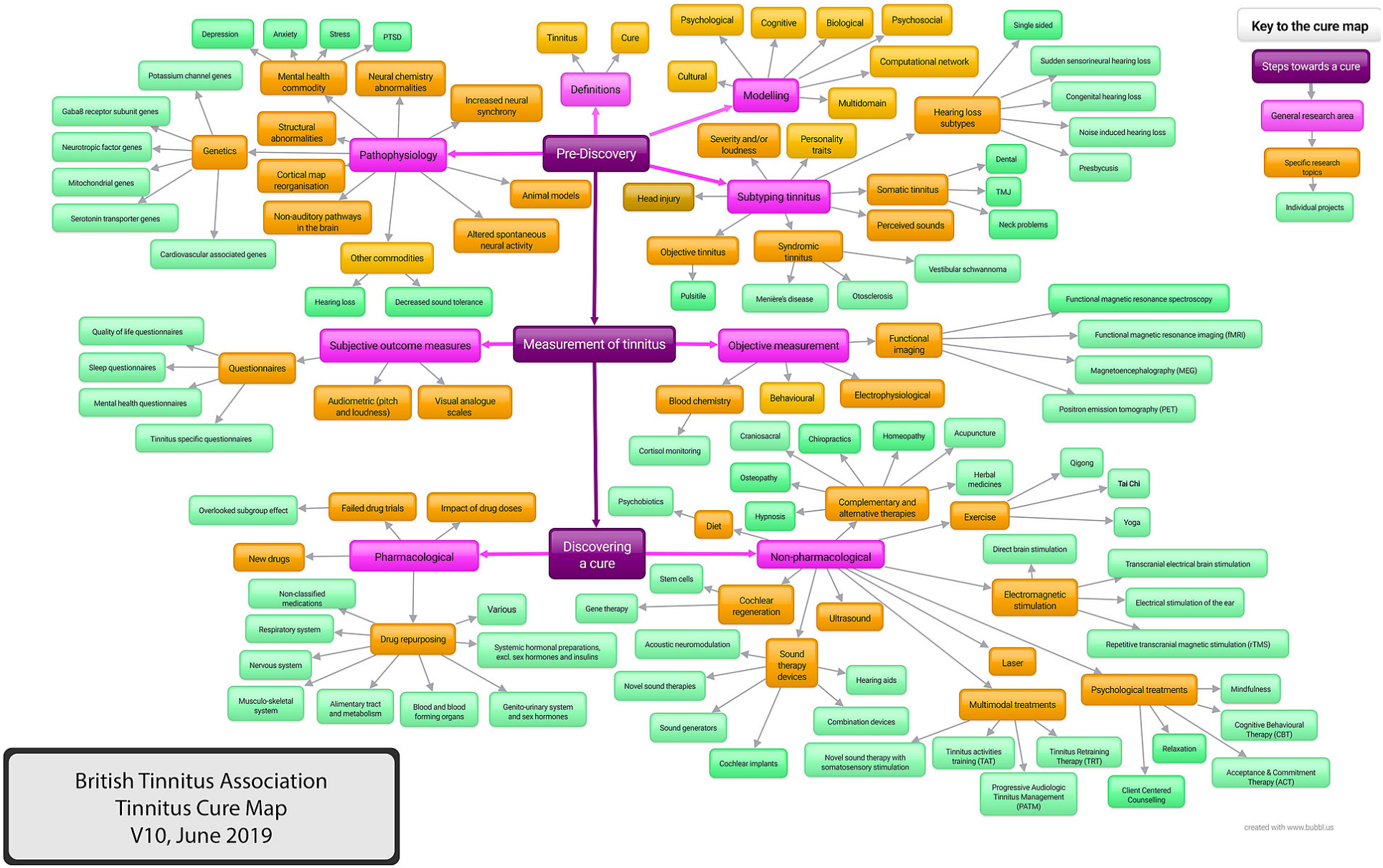


Cochlea

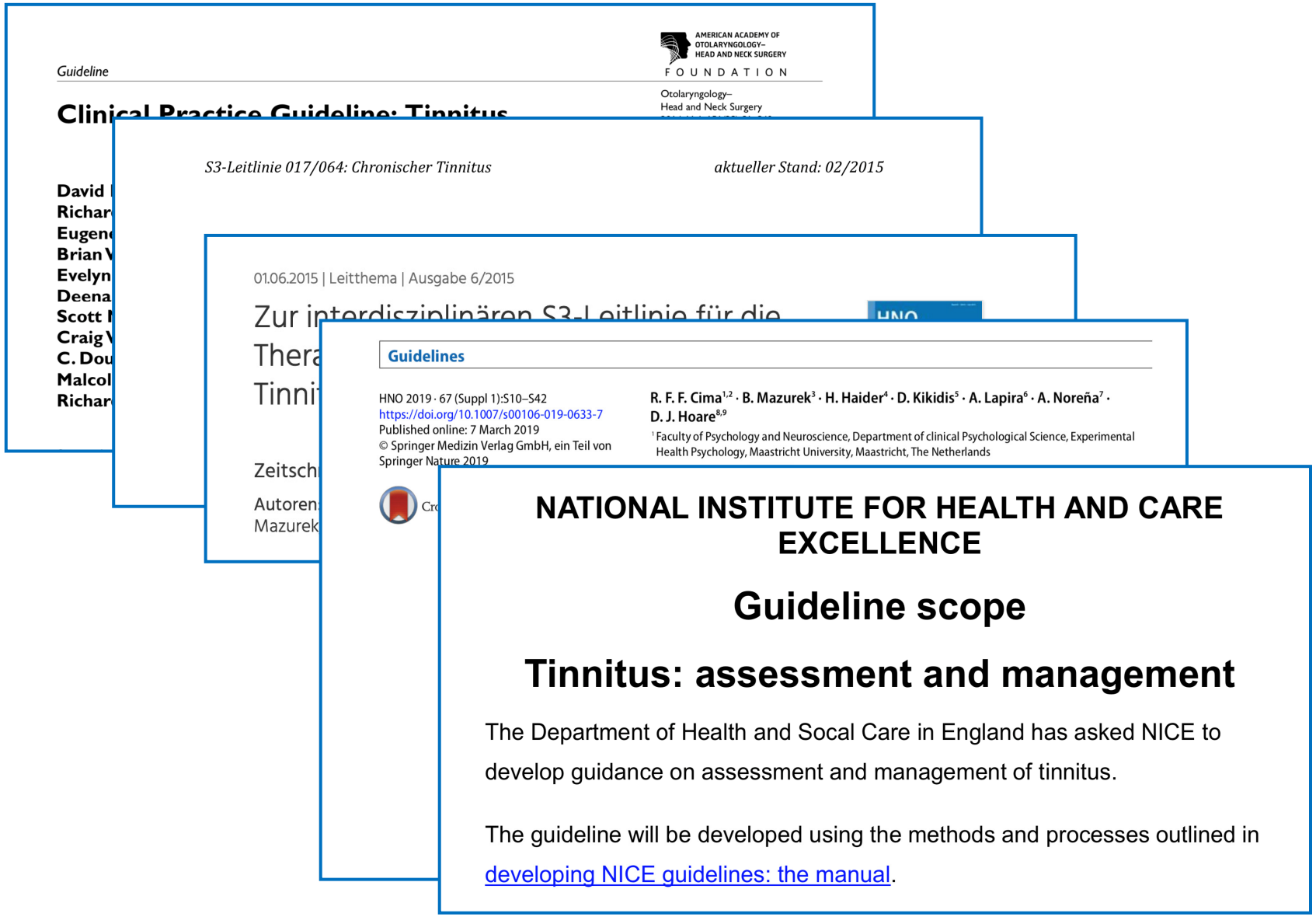
Central nervous system

führt zur Identifikation innovativer Therapieansätze

Shore, Roberts, Langguth Nat Rev Neurology 2016


Key to the cure map
Steps towards a cure
General research area
Specific research topics
Individual projects
Pre-Discovery
Definitions
Tinnitus
Cure
Pathophysiology
Mental health commodity
Depression
Anxiety
Stress
PTSD
Neural chemistry abnormalities
Genetics
Potassium channel genes
Gaba8 receptor subunit genes
Neurotropic factor genes
Mitochondrial genes
Serotonin transporter genes
Cardiovascular associated genes
Structural abnormalities
Cortical map reorganisation
Non-auditory pathways in the brain
Other commodities
Hearing loss
Decreased sound tolerance
Increased neural synchrony
Animal models
Altered spontaneous neural activity
Modelling
Psychological
Cognitive
Biological
Psychosocial
Cultural
Computational network
Multidomain
Severity and/or loudness
Personality traits
Subtyping tinnitus
Head injury
Objective tinnitus
Pulsitile
Syndromic tinnitus
Menière's disease
Otosclerosis
Vestibular schwannoma
Somatic tinnitus
Dental
TMJ
Neck problems
Perceived sounds
Hearing loss subtypes
Single sided
Sudden sensorineural hearing loss
Congenital hearing loss
Noise induced hearing loss
Presbycusis
Measurement of tinnitus
Subjective outcome measures
Questionnaires
Quality of life questionnaires
Sleep questionnaires
Mental health questionnaires
Tinnitus specific questionnaires
Audiometric (pitch and loudness)
Visual analogue scales
Objective measurement
Blood chemistry
Cortisol monitoring
Behavioural
Electrophysiological
Functional imaging
Functional magnetic resonance spectroscopy
Functional magnetic resonance imaging (fMRI)
Magnetoencephalography (MEG)
Positron emission tomography (PET)
Discovering a cure
Pharmacological
New drugs
Failed drug trials
Overlooked subgroup effect
Impact of drug doses
Drug repurposing
Non-classified medications
Respiratory system
Nervous system
Musculo-skeletal system
Alimentary tract and metabolism
Blood and blood forming organs
Genito-urinary system and sex hormones
Various
Systemic hormonal preparations, excl. sex hormones and insulins
Non-pharmacological
Complementary and alternative therapies
Craniosacral
Chiropractics
Homeopathy
Acupuncture
Osteopathy
Herbal medicines
Psychobiotics
Hypnosis
Diet
Exercise
Qigong
Tai Chi
Yoga
Cochlear regeneration
Stem cells
Gene therapy
Ultrasound
Sound therapy devices
Acoustic neuromodulation
Novel sound therapies
Sound generators
Cochlear implants
Hearing aids
Combination devices
Electromagnetic stimulation
Direct brain stimulation
Transcranial electrical brain stimulation
Electrical stimulation of the ear
Repetitive transcranial magnetic stimulation (rTMS)
Laser
Multimodal treatments
Novel sound therapy with somatosensory stimulation
Tinnitus activities training (TAT)
Tinnitus Retraining Therapy (TRT)
Progressive Audiologic Tinnitus Management (PATM)
Psychological treatments
Mindfulness
Cognitive Behavioural Therapy (CBT)
Relaxation
Acceptance & Commitment Therapy (ACT)
Client Centered Counselling
British Tinnitus Association
Tinnitus Cure Map
V10, June 2019
created with www.bubbl.us

Leitlinien zur Behandlung von Tinnitus



Niedrige methodische Standards

Prog Brain Res. 2007 ; 166: 525–536. doi:10.1016/S0079-6123(07)66050-6.

Consensus for tinnitus patient assessment and treatment outcome measurement: Tinnitus Research Initiative meeting, Regensburg, July 2006

B. Langguth[1,*], R. Goodey[2], A. Azevedo[3], A. Bjorne[4], A. Cacace[5], A. Crocetti[6], L. Del Bo[6], D. De Ridder[7], I. Diges[8], T. Elbert[9], H. Flor[10], C. Herraiz[8], T. Ganz Sanchez[11], P. Eichhammer[1], R. Figueiredo[3], G. Hajak[1], T. Kleinjung[12], M. Landgrebe[1], A. Londero[13], M.J.A. Lainez[14], M. Mazzoli[15], M.B. Meikle[16], J. Melcher[17], J.P. Rauschecker[18], P.G. Sand[1], M. Struve[10], P. Van de Heyning[19], P. Van Dijk[20], and R. Vergara[21]

J Psychosom Res. 2012 August ; 73(2): 112–121. doi:10.1016/j.jpsychores.2012.05.002.

Methodological aspects of clinical trials in tinnitus: A proposal for an international standard

Michael Landgrebe[1,2,*], Andréia Azevedo[3], David Baguley[4], Carol Bauer[5], Anthony Cacace[6], Claudia Coelho[7], John Dornhoffer[8], Ricardo Figueiredo[3], Herta Flor[9], Goeran Hajak[10], Paul van de Heyning[11], Wolfgang Hiller[12], Eman Khedr[13], Tobias Kleinjung[14], Michael Koller[15], Jose Miguel Lainez[16], Alain Londero[17], William H. Martin[18], Mark Mennemeier[19], Jay Piccirillo[20], Dirk De Ridder[21], Rainer Rupprecht[1], Grant Searchfield[22], Sven Vanneste[21], Florian Zeman[15], and Berthold Langguth[1,2]

Outcome Measurement is complex

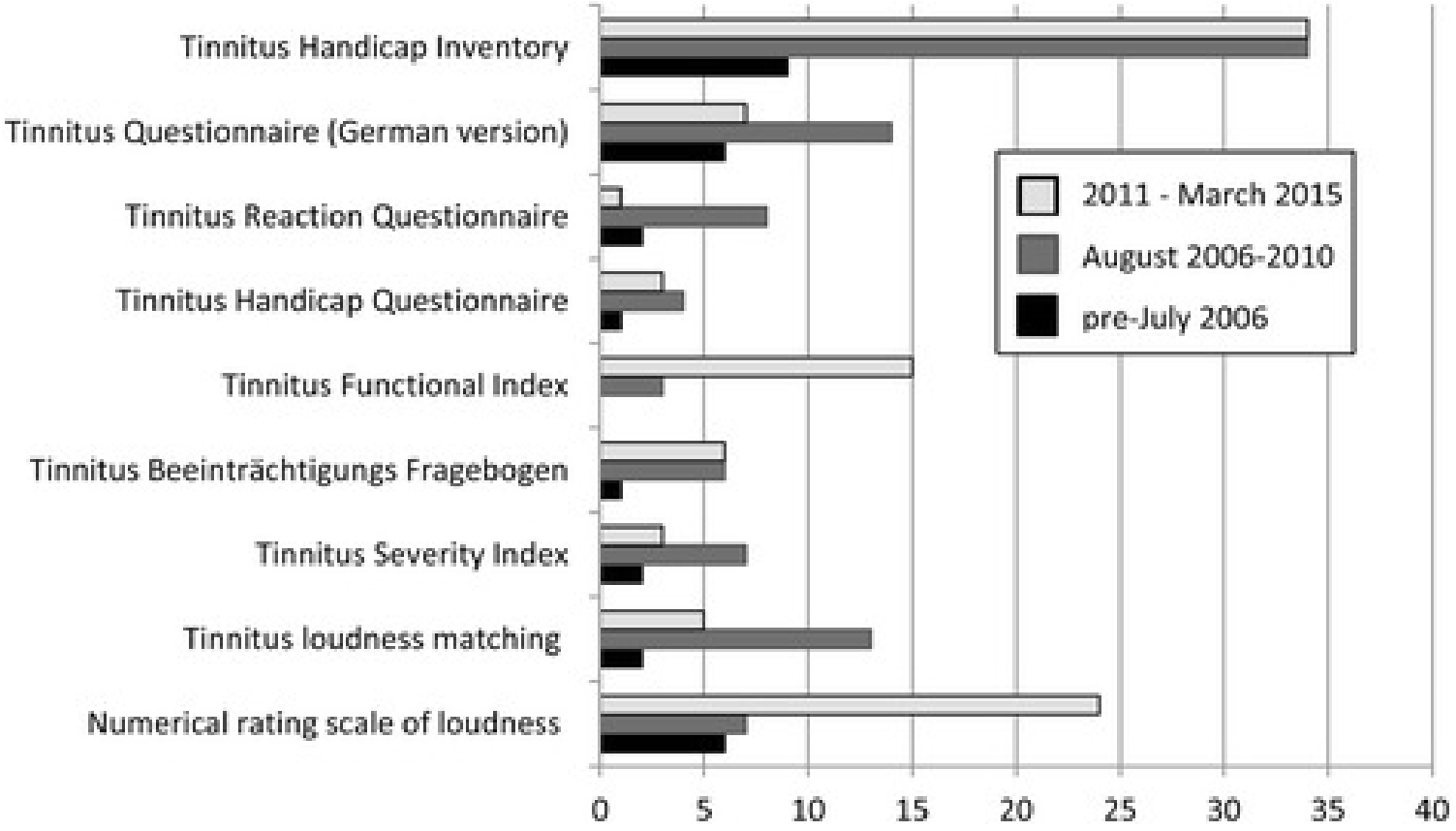
Tinnitus is a subjective phenomenon

- Best validity / reliability for Questionnaires
  - even if most Questionnaires were not designed for the assessment of changes
- Tinnitus loudness can be assessed by visual analogue or numeric rating scales
- Psychoacoustic measurements (Loudness match, minimal masking levels) not very reliable

Tinnitus can fluctuate over time

- Smart-phone Apps seem useful for ecological momentary assessment

Outcome Measurement ist komplex

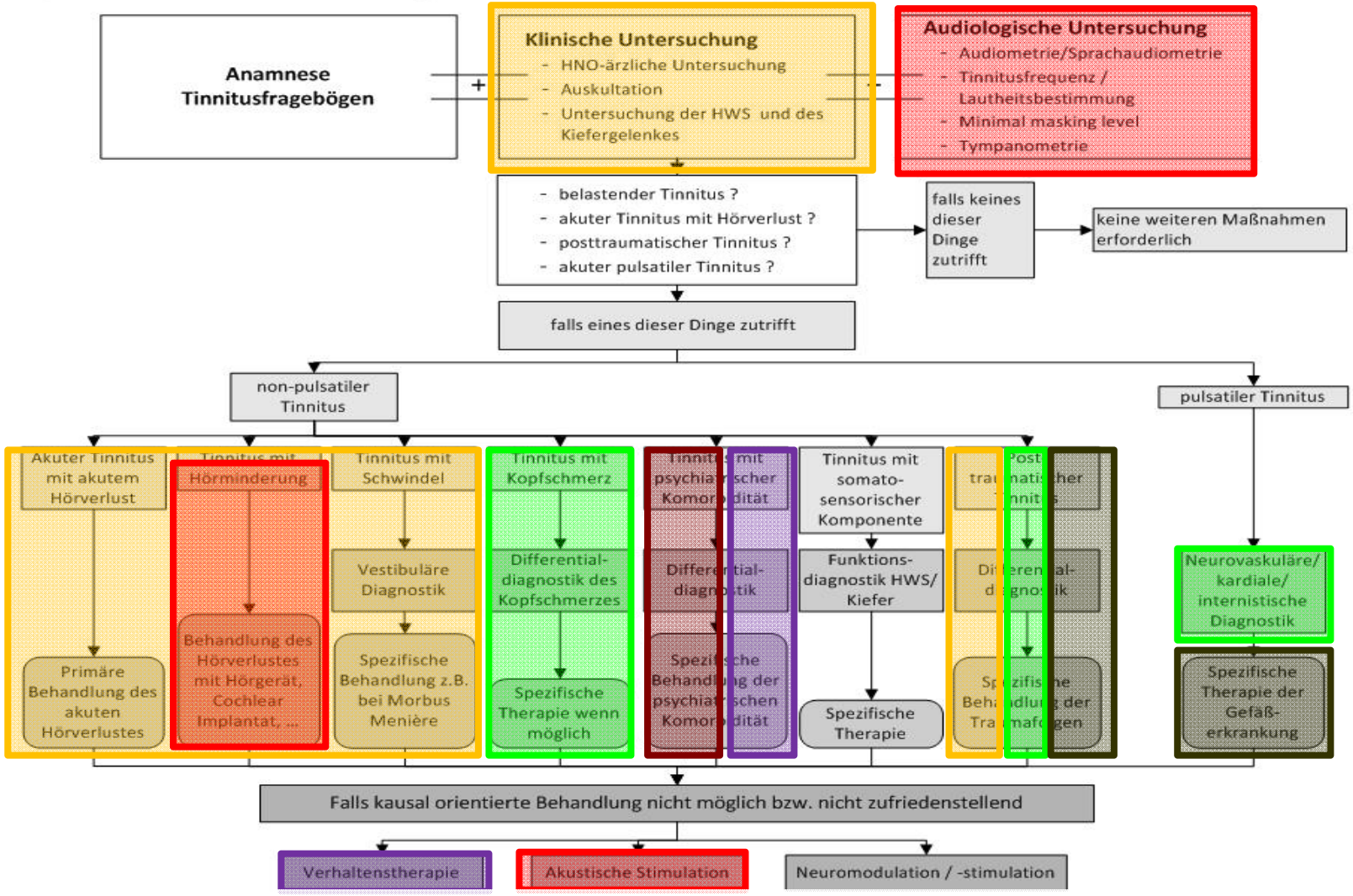


Vielfältige Methoden sind in Verwendung

(Hall et al. 2016)

HNO | Audiologe | Neurologe | Neurochirurg | Psychiater | Psychotherapeut

Algorithmus zur Diagnose und Therapie des chronischen Tinnitus



Notwendigkeit der Behandlung im multidiziplinären Verbund

Allgemeine Empfehlungen I

Ein neu auftretender Tinnitus sollte diagnostisch abgeklärt werden

Insbesondere sollte das Hörvermögen untersucht werden

Wenn der Tinnitus nicht stört und keine Belastung darstellt, dann braucht er nicht behandelt zu werden

Klinische Einteilung der Schweregrade bei Tinnitus

Die Einteilung der Tinnitus-Schweregrade nach Biesinger et al. (e30) ist klinisch-praktisch ausgerichtet und berücksichtigt die Auswirkung des Ohrgeräusches im beruflichen und privaten Bereich.

Grad 1: Der Tinnitus ist gut kompensiert, kein Leidensdruck.
Grad 2: Der Tinnitus tritt hauptsächlich in der Stille auf und wirkt störend bei Stress und Belastungen.
Grad 3: Der Tinnitus führt zu einer dauernden Beeinträchtigung im privaten und beruflichen Bereich. Es treten Störungen im emotionalen, kognitiven und körperlichen Bereich auf.
Grad 4: Der Tinnitus führt zur völligen Dekompensation im privaten Bereich und zur Berufsunfähigkeit.

Woody Allen, «Hannah und ihre Schwestern», 1986


Ich halte den Tinnitus nicht mehr aus !
Ich will dass er aufhört !
Wegen dem Tinnitus kann ich nicht mehr schlafen !
Ich kann mich nicht daran gewöhnen
Ich bin verzweifelt !

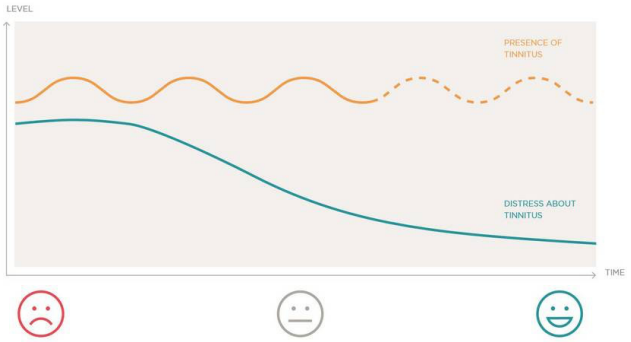
Offenkundige Hilflosigkeit

Der Patient fühlt sich unverstanden und alleine gelassen

Herstellung einer theraputischen Beziehung und Vermittlung von Hoffnung

Allgemeine Empfehlungen II

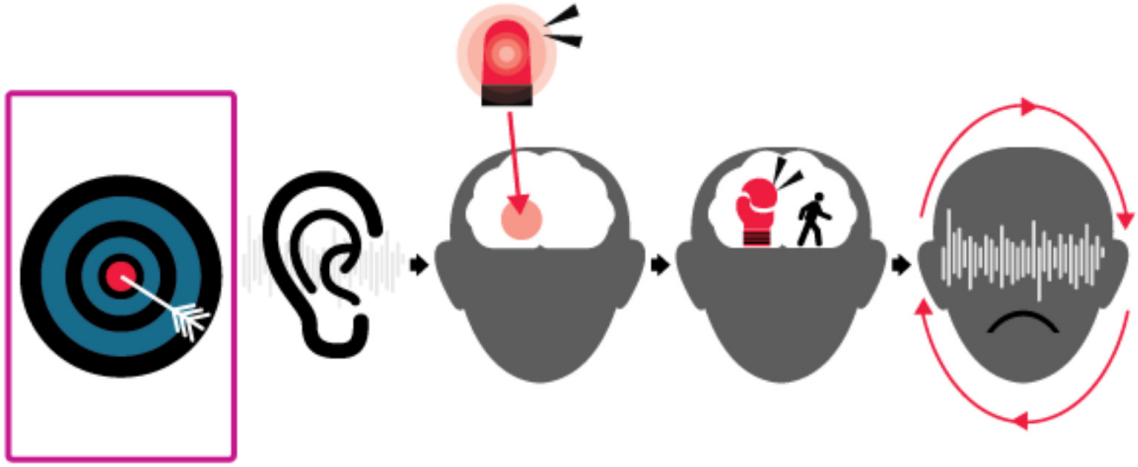
Information:
- Tinnitus ist nicht gefährlich
- Die Tinnitusbelastung wird im Laufe der Zeit weniger
- Die Reaktion auf den Tinnitus und das Tinnitusgeräusch sind nicht identisch



Gezielte Ablenkung ist hilfreich:
- Hintergrundgeräusche
- Musik
- Zimmerspringbrunnen
- Aktivitäten

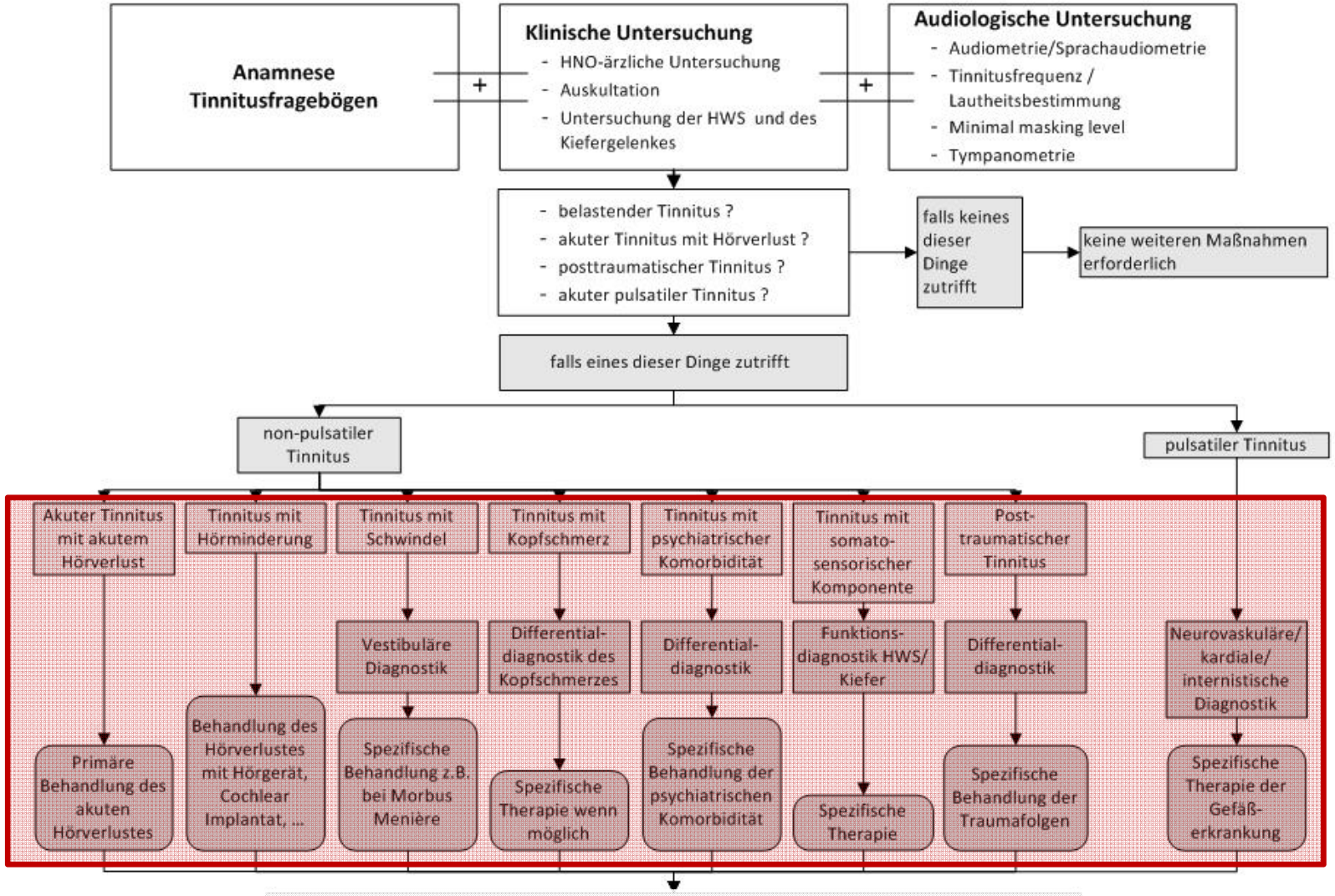
Ko-morbiditäten wie Schlafstörungen oder Depression sind gut behandelbar, selbst wenn das Tinnitusgeräusch bestehen bleibt

Seriöse Information über therapeutische Möglichkeiten



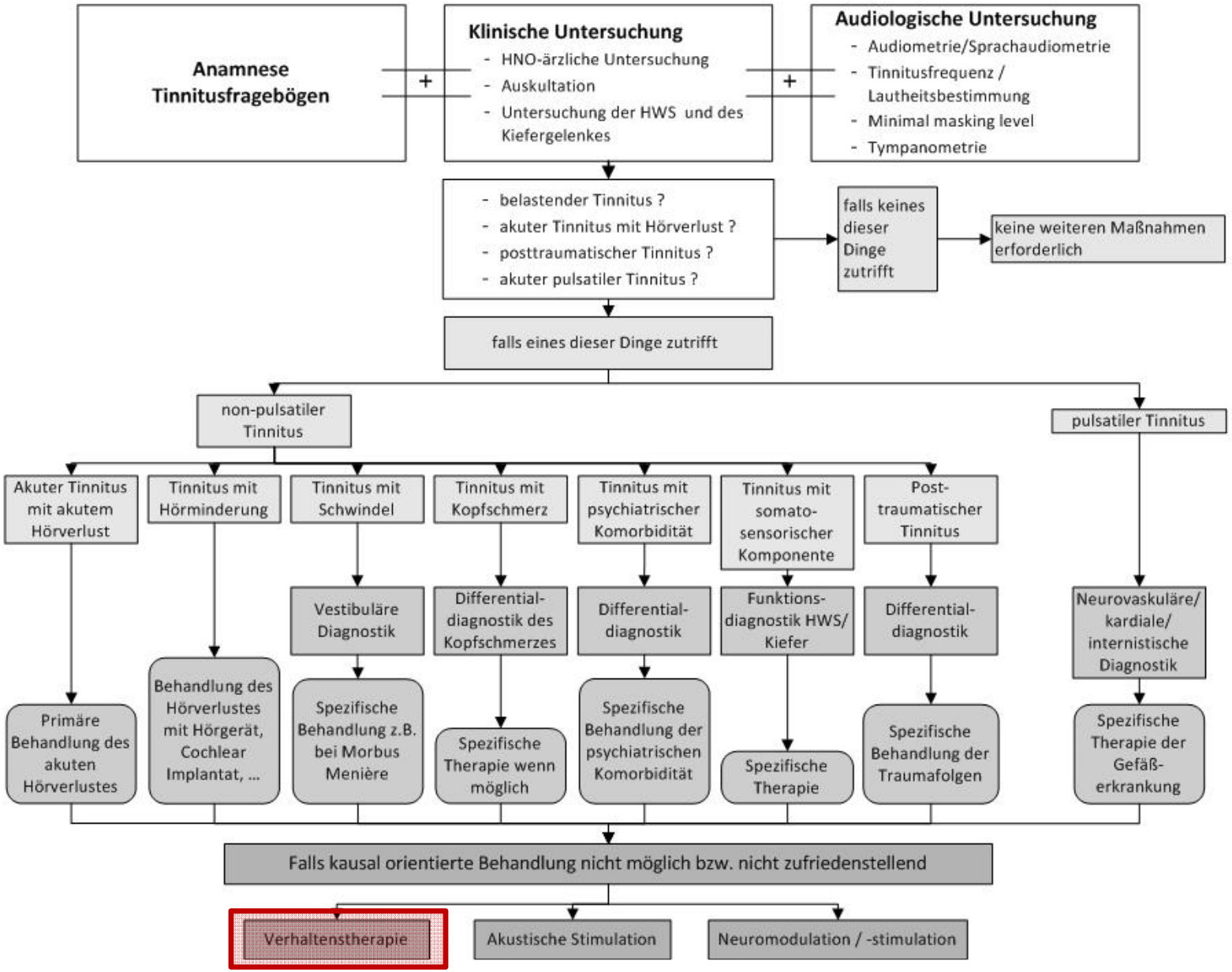

1
2
3
1
2
3

Algorithmus zur Diagnose und Therapie des chronischen Tinnitus



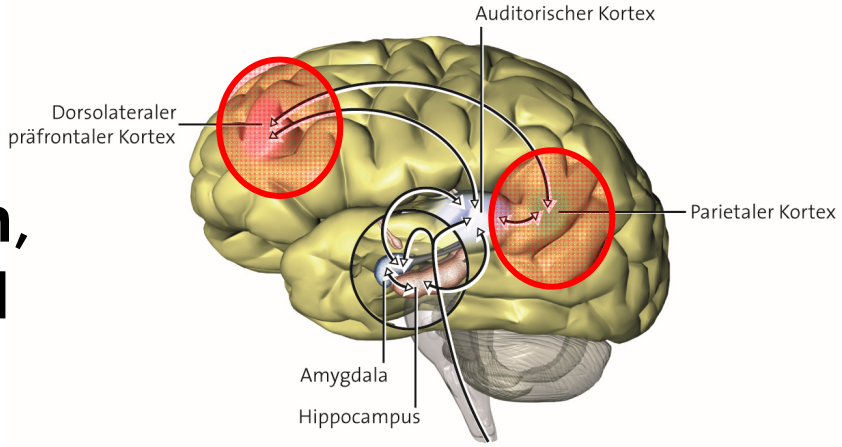
Diagnostische Abklärung und Behandlung von spezifschen Formen von Tinnitus und Komorbidtäten

Algorithmus zur Diagnose und Therapie des chronischen Tinnitus



Verhaltenstherapie

Ziel:
Redukton der Verknüpfung zwischen auditorischem System, Aufmerksamkeitssteuerung und Stressnetzwerk



Die Wirksamkeit der kognitiven Verhaltenstherapie auf den subjektiven Tinnitusschweregrad ist durch Cochrane-Metaanalysen belegt.

Martinez Devesa et al. 2007, 2010

Verhaltenstherapie

Verschiedene Inhalte

- Kognitive Restrukturierung
- Exposition
- Acceptance and Commitment (ACT)
- MBSR (mindfulness)
- Techniken zur Aufmerksamkeitsumlenkung
- Stressmanagement
- Entspannungstechniken

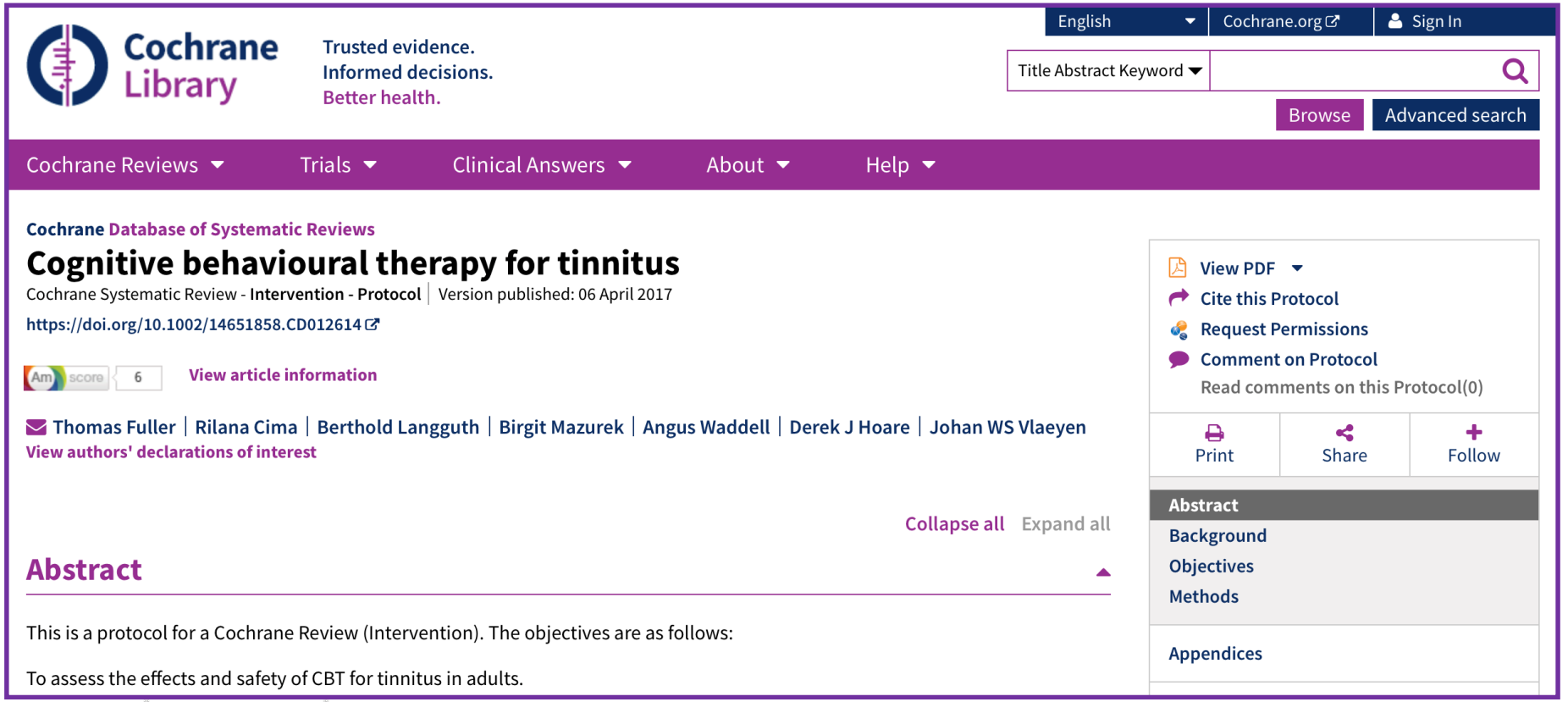
Verschiedene Settings

- Einzeltherapie
- Grupentherapie
- Online-basiert

Verhaltenstherapie

Verschiedene Inhalte

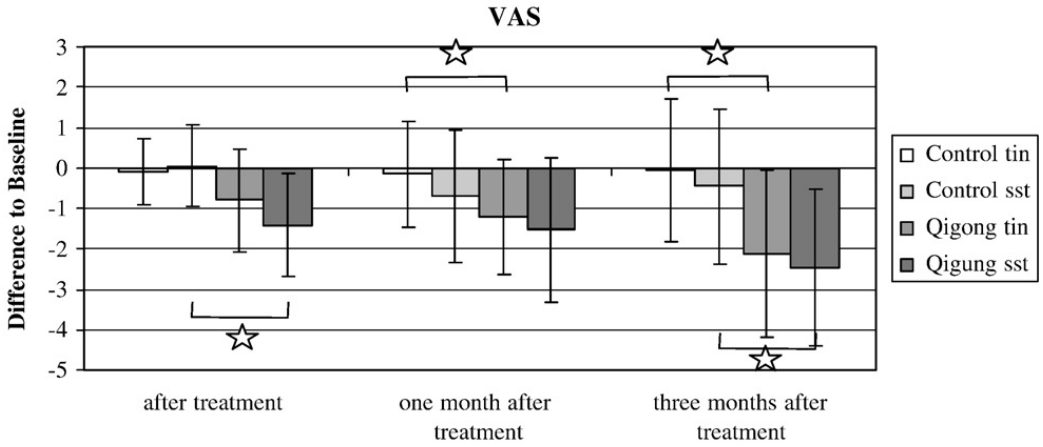
- Kognitive Restrukturierung



- Online-basiert

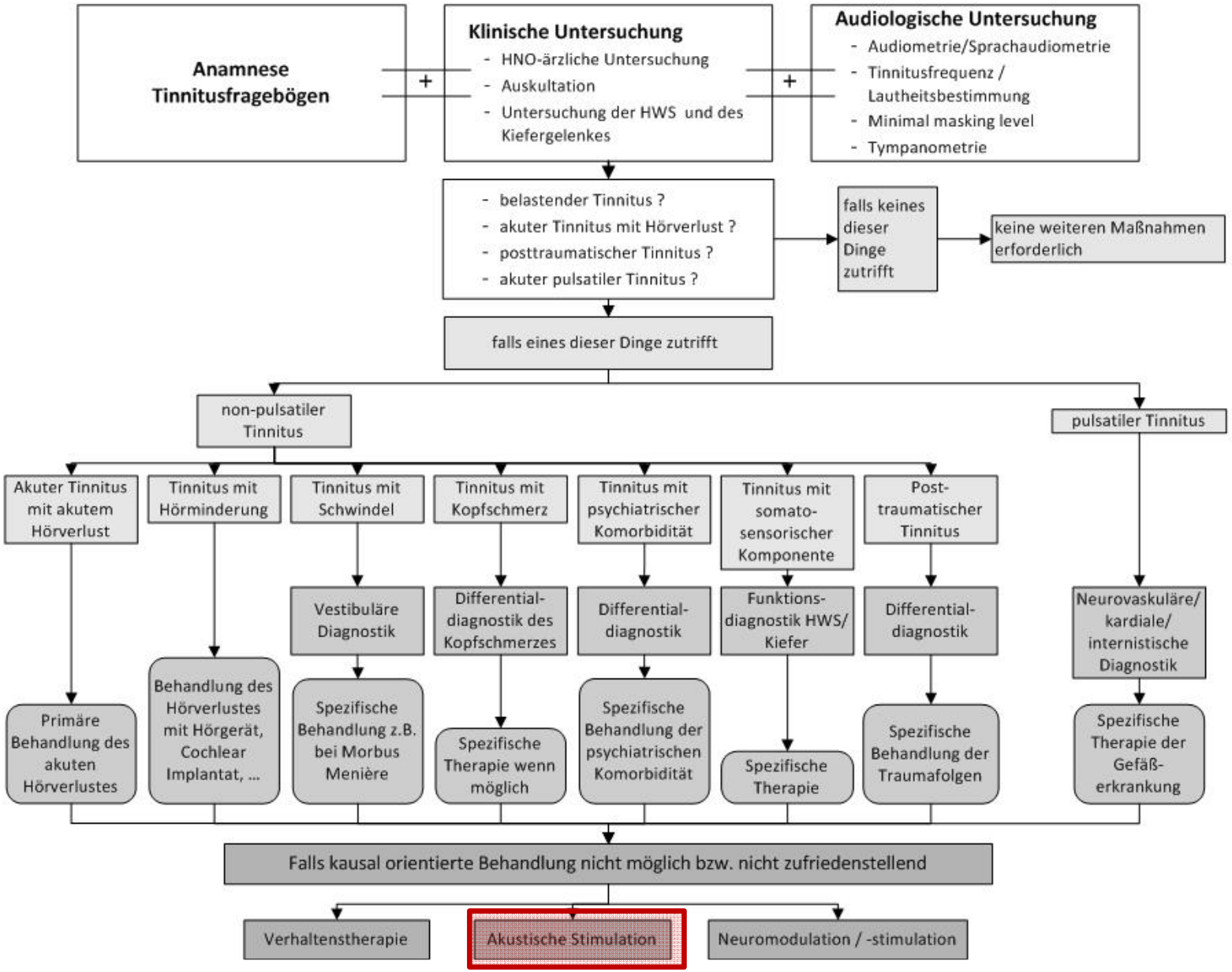
Entspannungstechniken

aktive Verfahren, wie z.B. QiGong fallen Tinnituspatienten in der Regel leichter

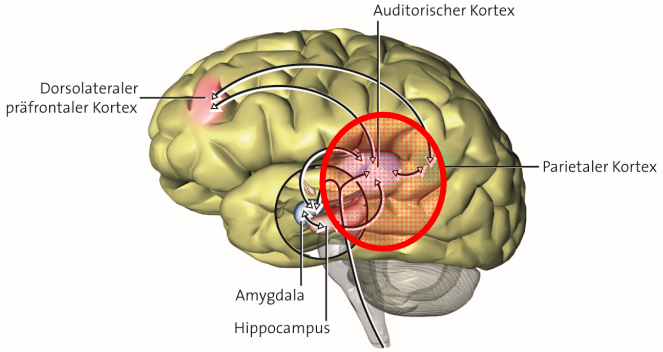


Biesinger et al. J Psychsom. Res. 2010

Algorithmus zur Diagnose und Therapie des chronischen Tinnitus



Hörgeräte


Auditorischer Kortex
Dorsolateraler präfrontaler Kortex
Parietaler Kortex
Amygdala
Hippocampus

Sound Therapie

- Tinnitus wird in den meisten Fällen maskiert durch andere Geräusche
- Maskierung ist dann sinnvoll, wenn die maskierenden Geräusche angenehmer sind als der Tinnitus
- Noiser, auch integriert in Hörgeräte
- Hintergrundgeräusche
  - Zimmerspringbrunnen
  - Musik
  - Naturgeräusche

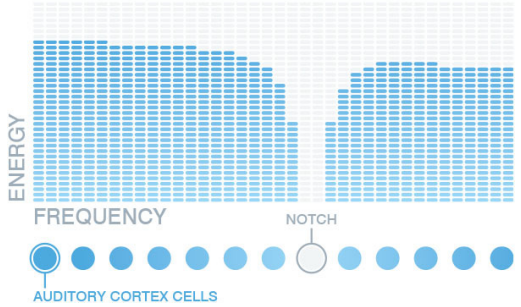
Am besten ist, was subjektiv am angenehmsten ist

Spezifische akustische Stimulation

Individualisierte akustische Stimulation:

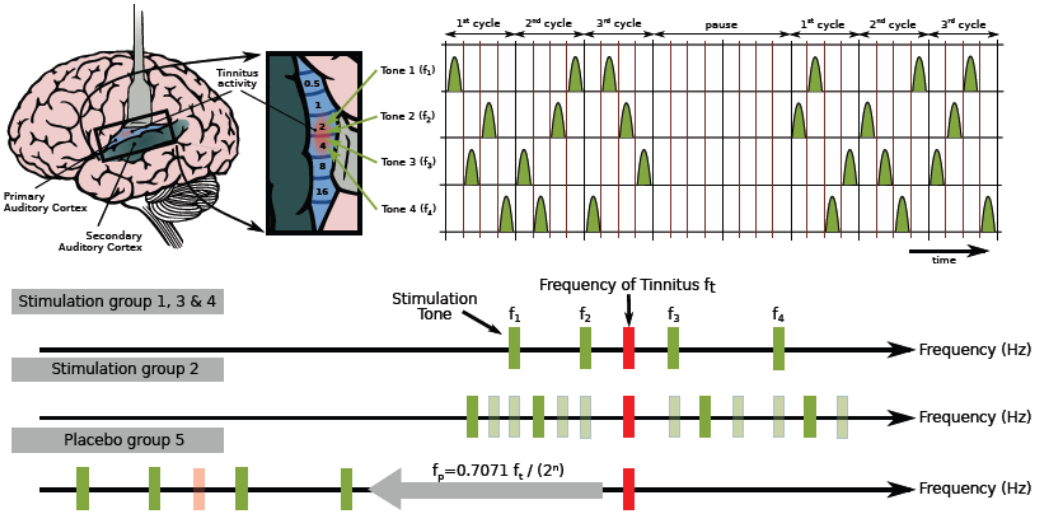
Gezielte akustische Stimulation mit Ausfiltering der Tinnitusfrequenz

Okamoto et al. 2010



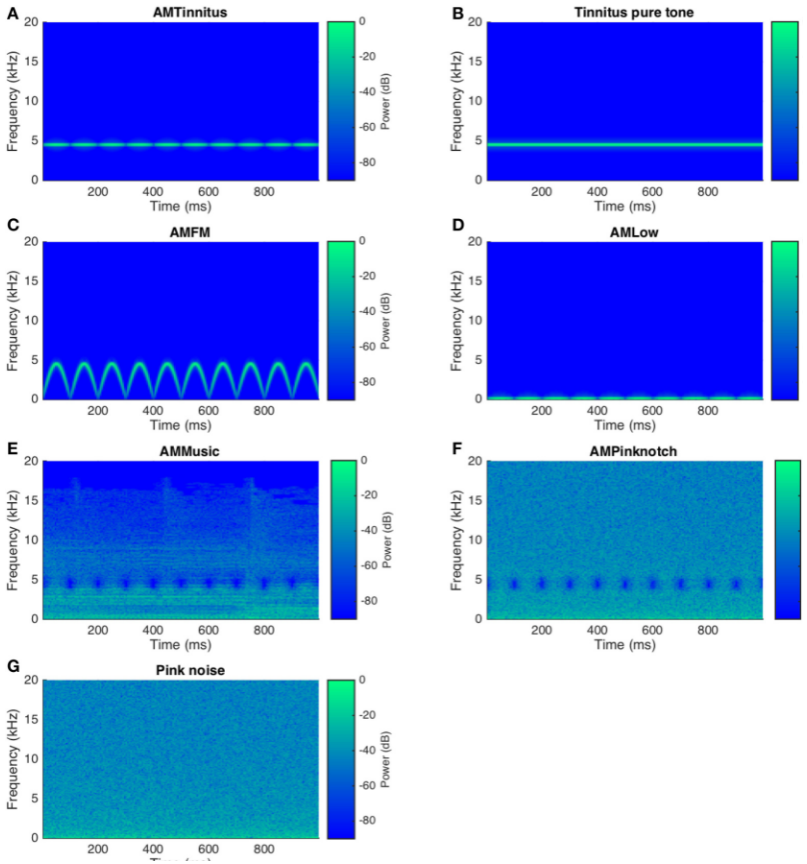
Desynchronisierende akustische Stimulation

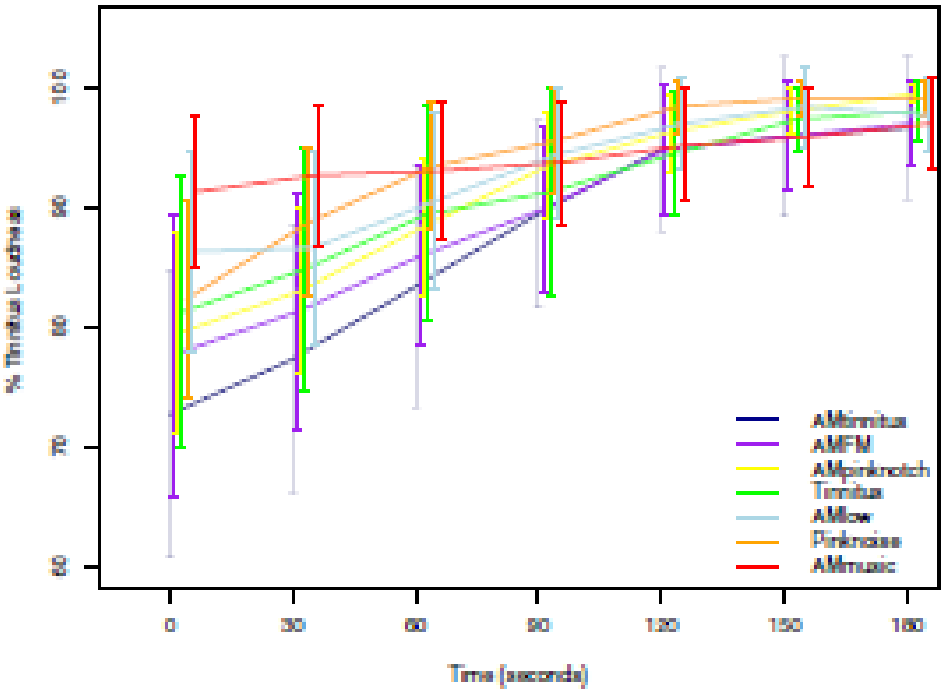
Tass et al. 2012



Spezifische akustische Stimulation

Gezielte akustische Stimulation:

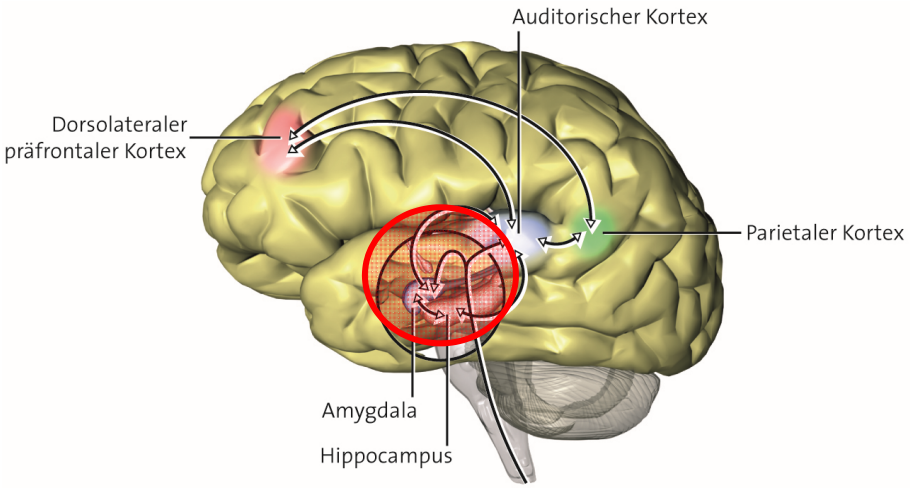




Neff et al. 2019

Gehirnstimulation

Auditorisches System:



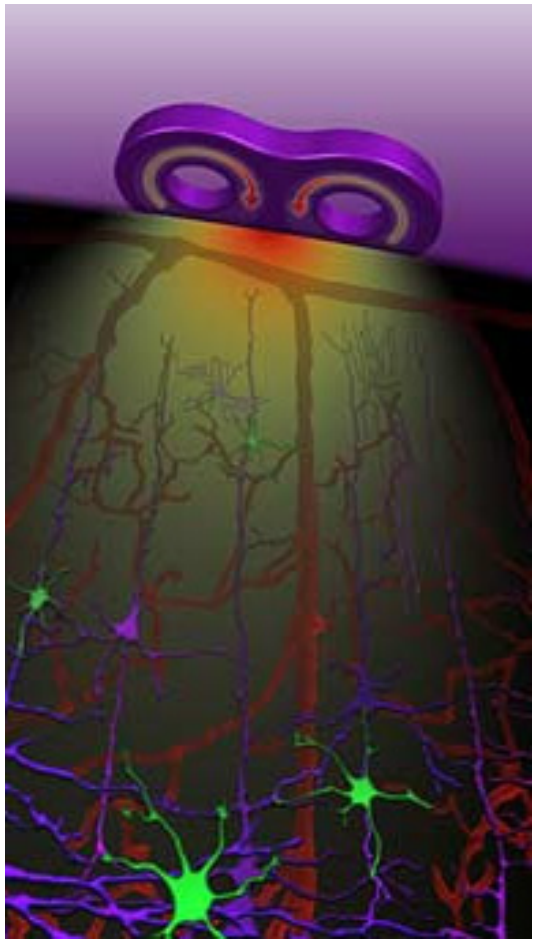
Transkranielle Magnetstimulation des auditorischen Kortex

Langguth et al. 2008

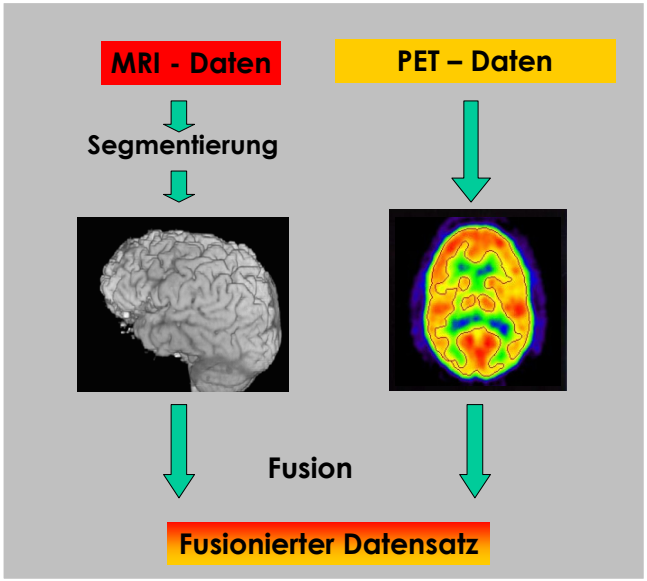
Transkranielle Magnetstimulation

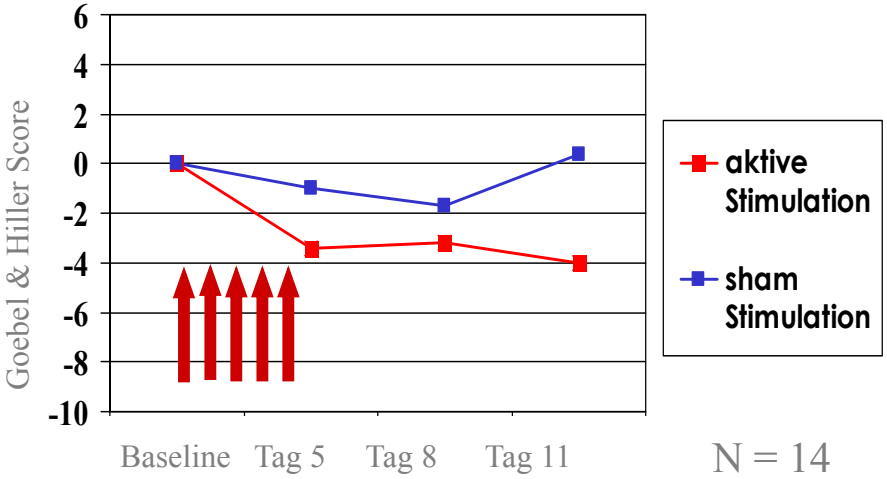
Schmerzlose
nichtinvasive

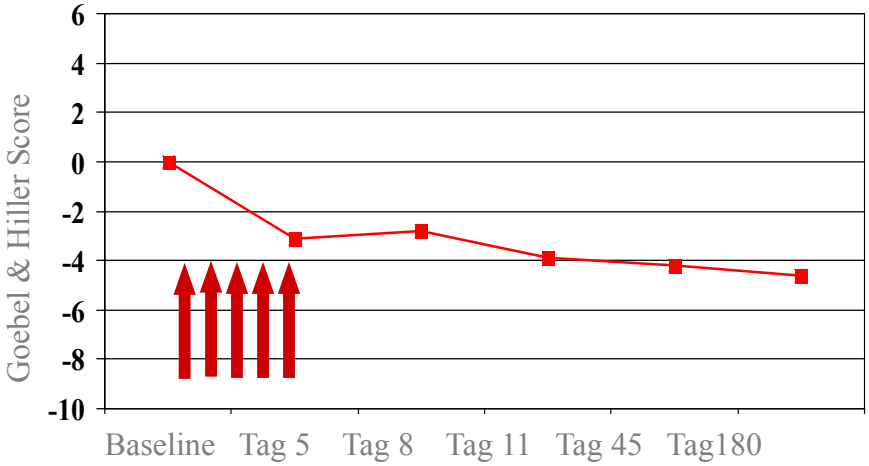
Modulation
von
Gehirnaktivität



Repeated TMS session result in lasting tinnitus reduction

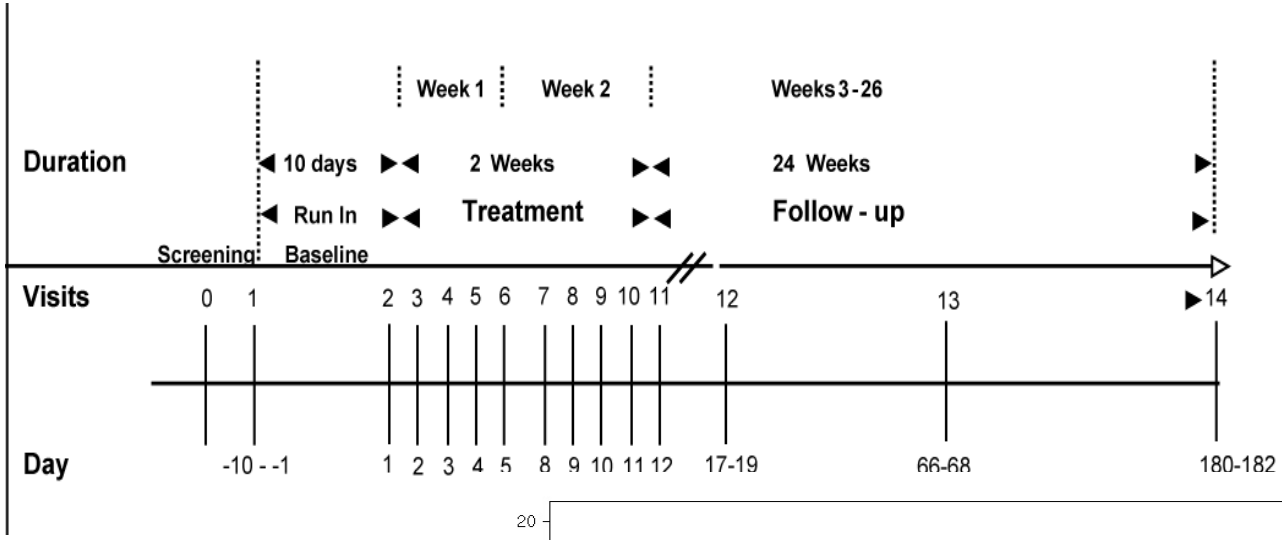




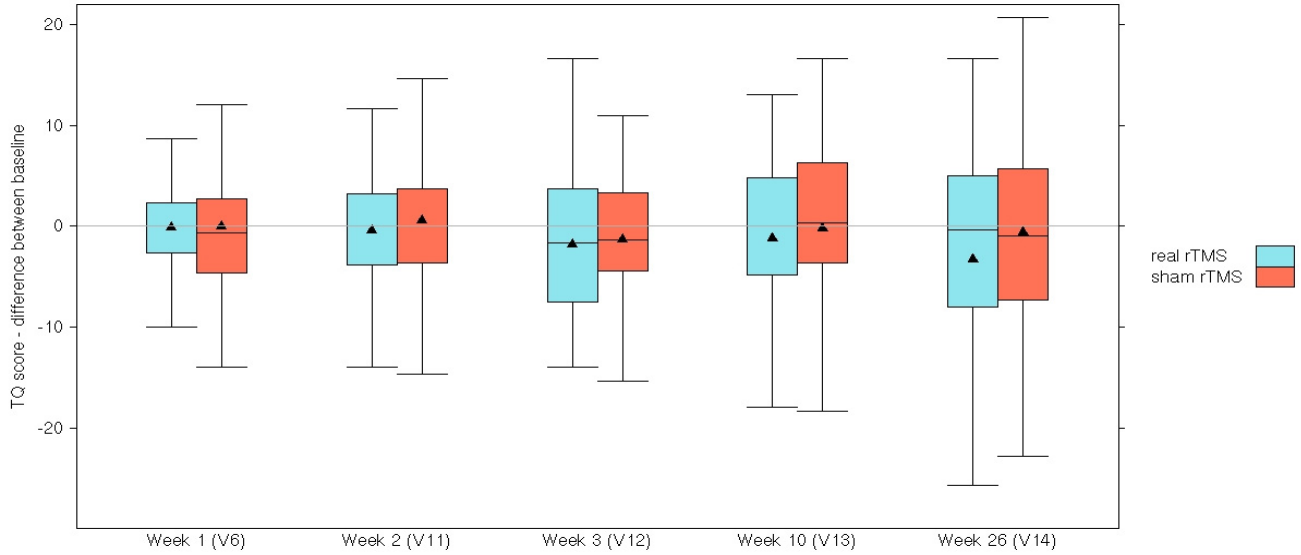


Kleinjung et al. Otol Head Neck Surg, 2005
Langguth et al. BMC Neuroscience, 2007

1 Hz rTMS des linken audtorischen Kortex

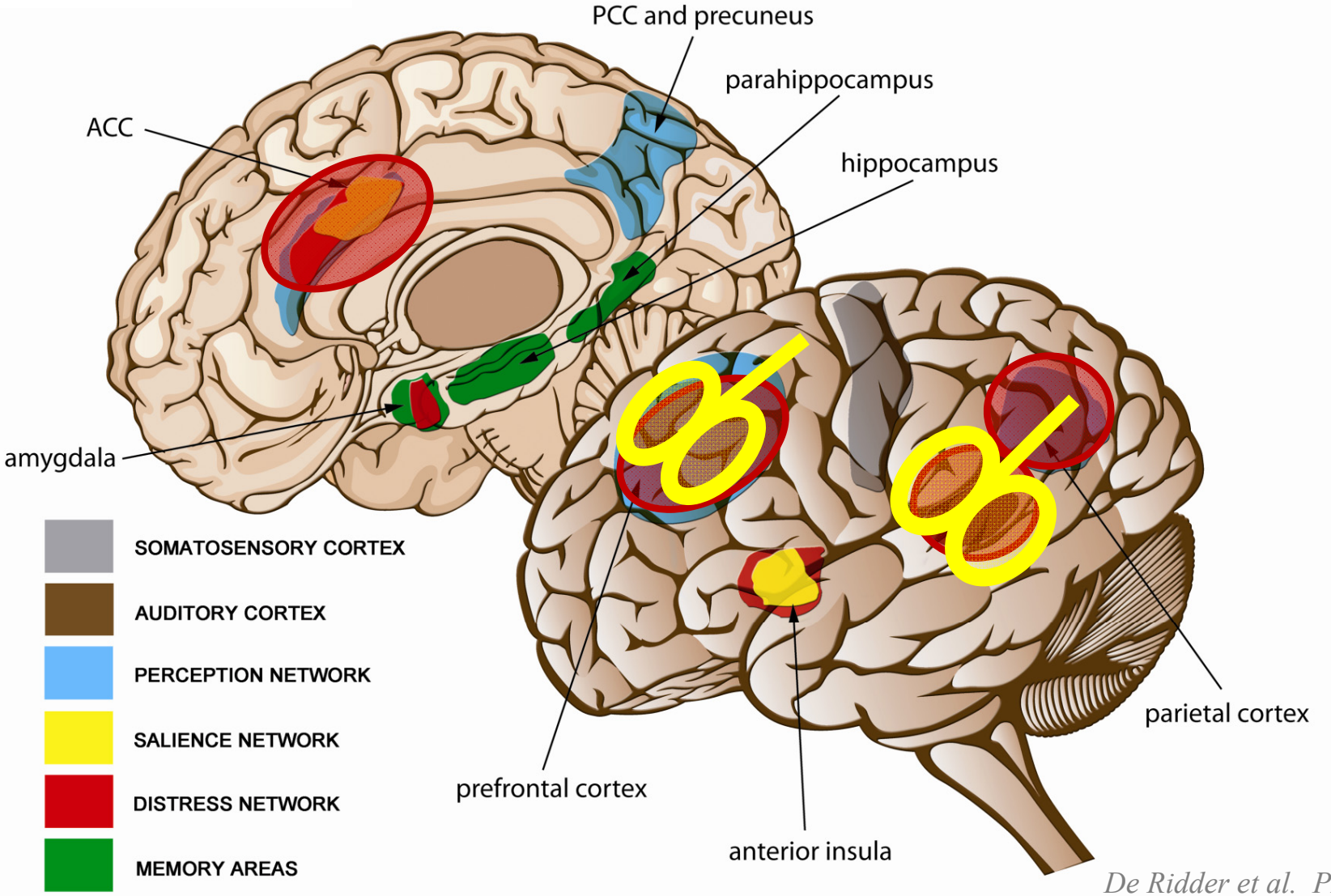


N = 153



Landgrebe et al. 2017

Stimulation verschiedener Zielareale



De Ridder et al. PNAS 2011

Langguth et al. Lancet Neurology 2013

Frontale + temporale Stimulation

N = 32

„temporal“:	„frontal + temporal“:
2000 St @ 1 Hz links temporal	1000 St @ 20 Hz links DLPFC + 1000 St @ 1 Hz links temporal

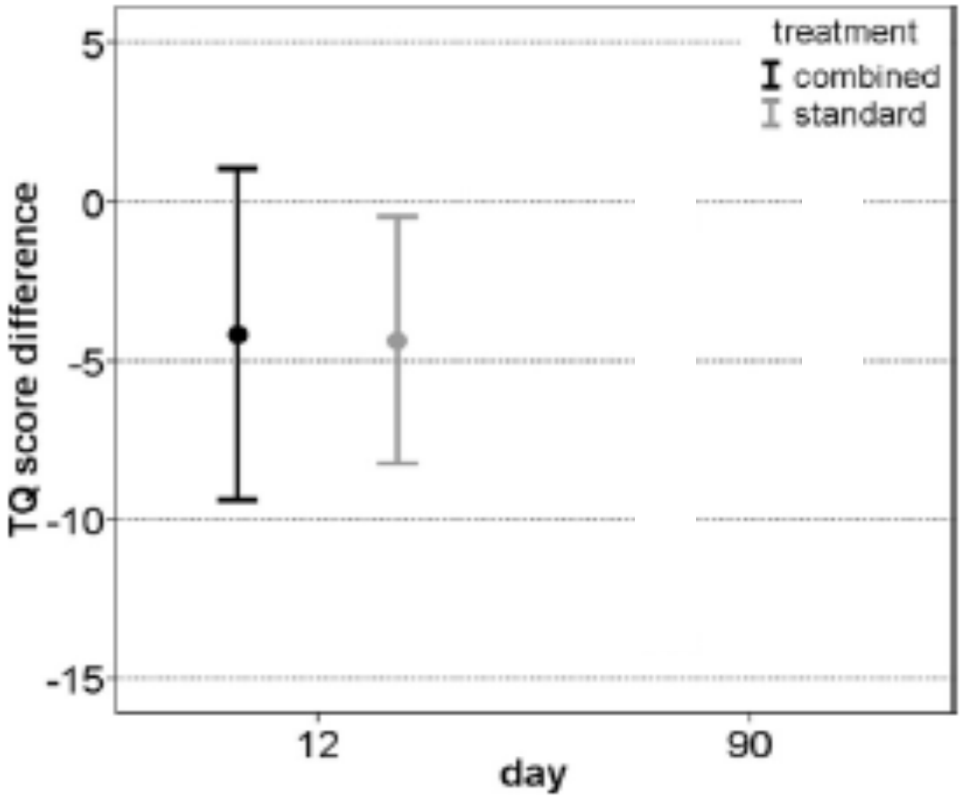
10 Tage aktive rTMS,

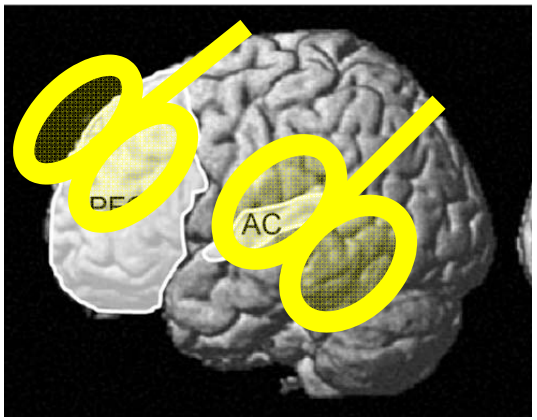
3 Monate follow up

Outcome – Parameter: Tinnitus - Fragebogen

Kleinjung et al., 2008

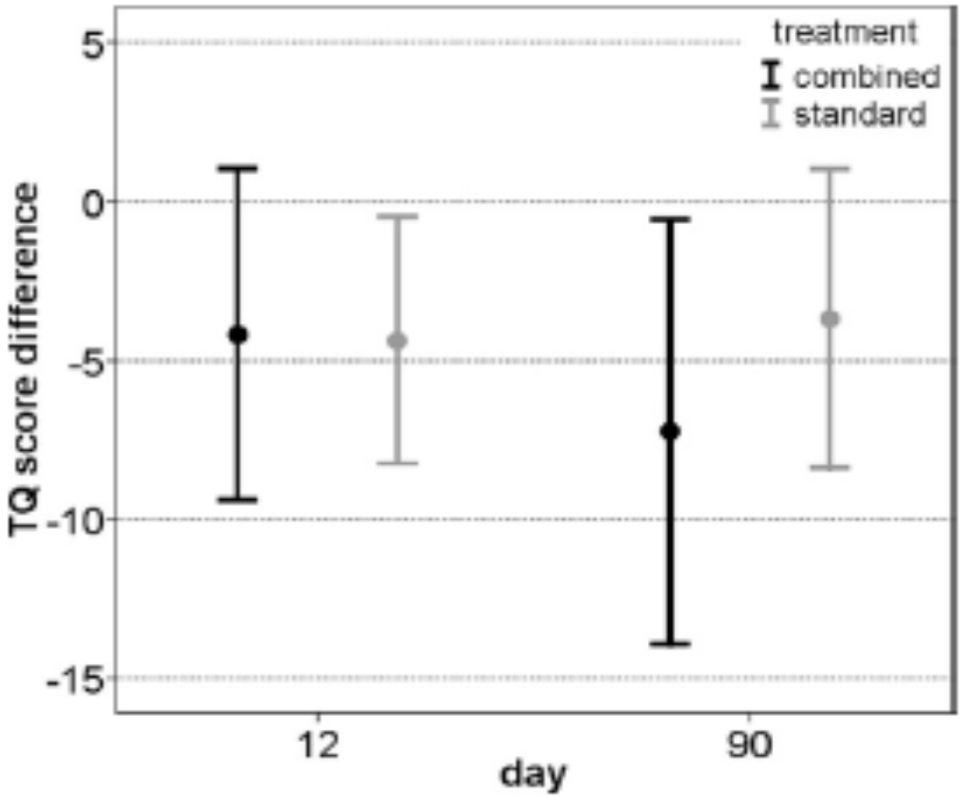
Frontale + temporale Stimulation

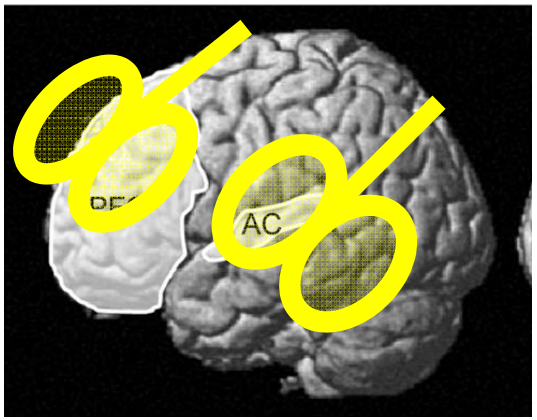




Kleinjung et al., 2008

Frontale + temporale Stimulation

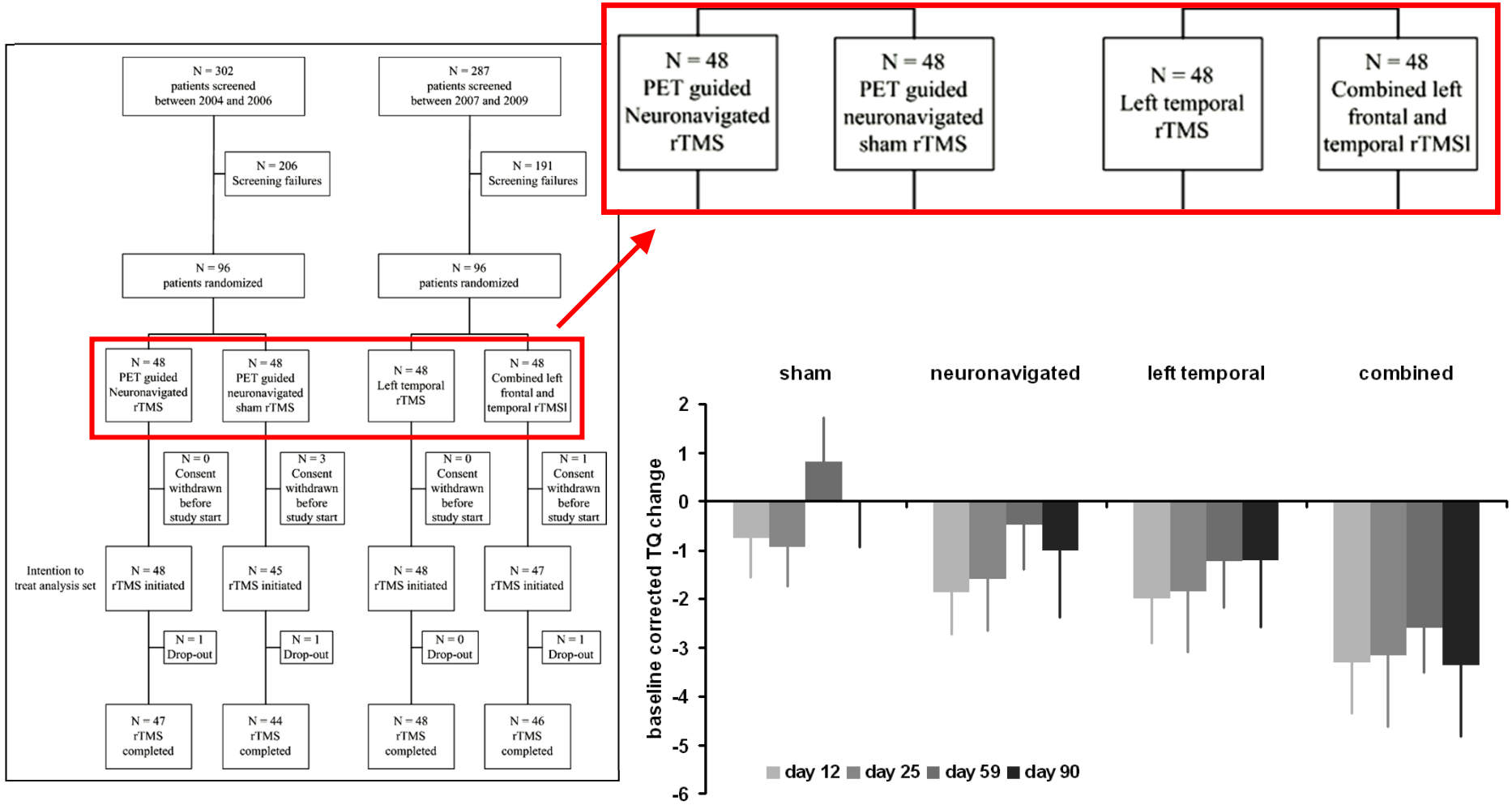




Ausgeprägtere Reduktion der Tinnitusbelastung in der Follow-up Phase nach kombinierter Stimulation

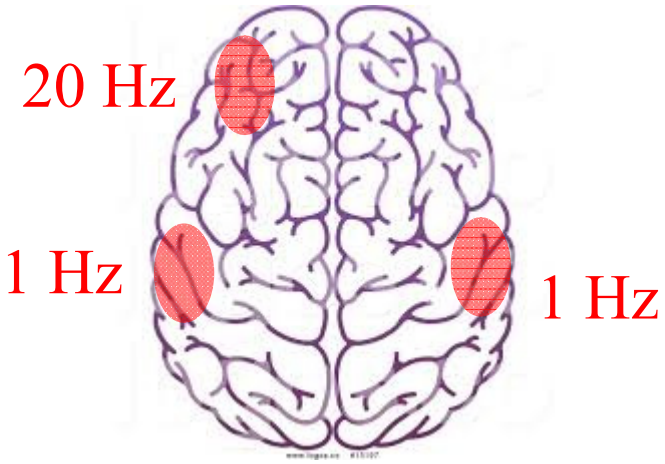
Kleinjung et al., 2008

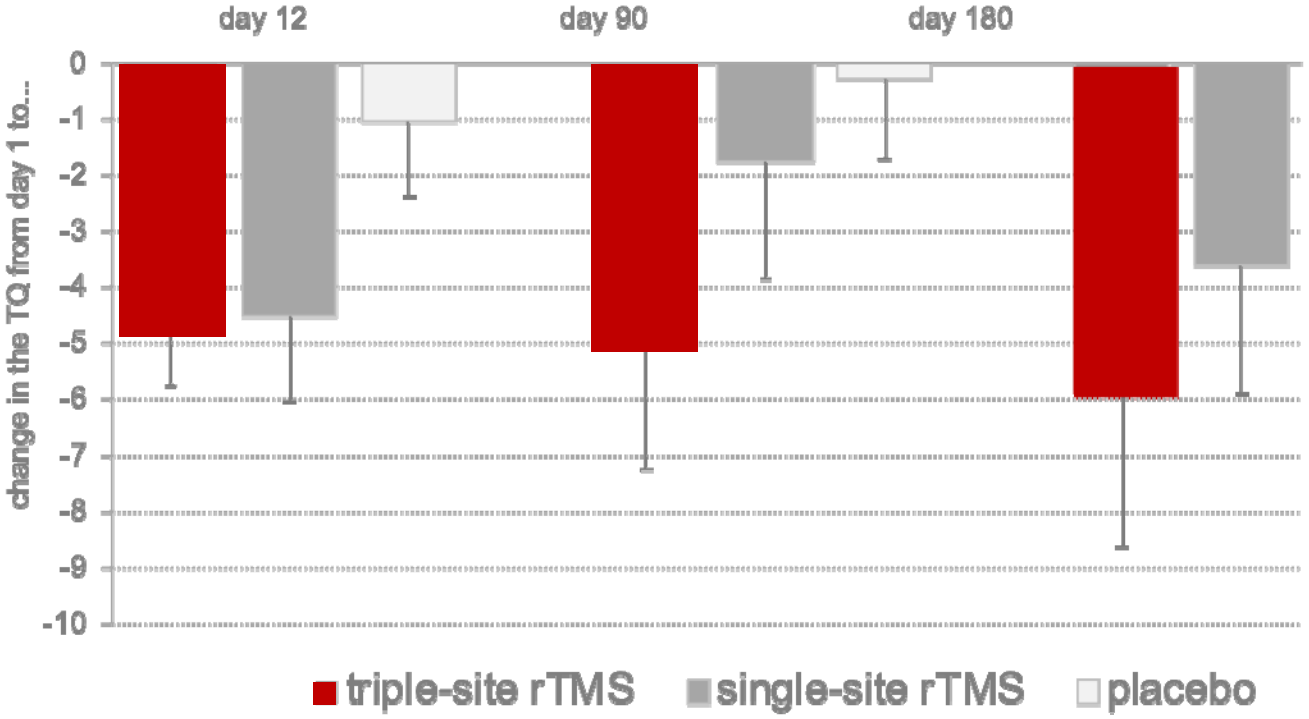
Frontale + temporale Stimulation



Langguth et al., 2012

Triple TMS





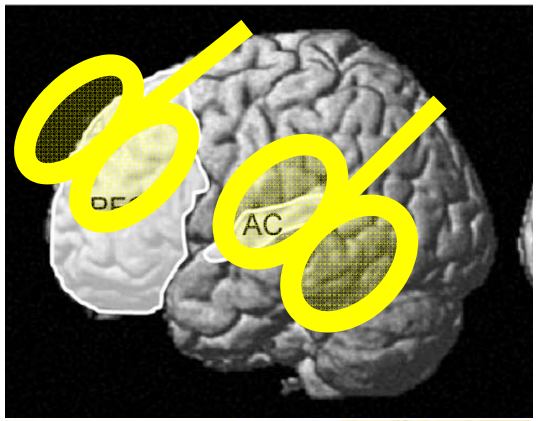
N = 50

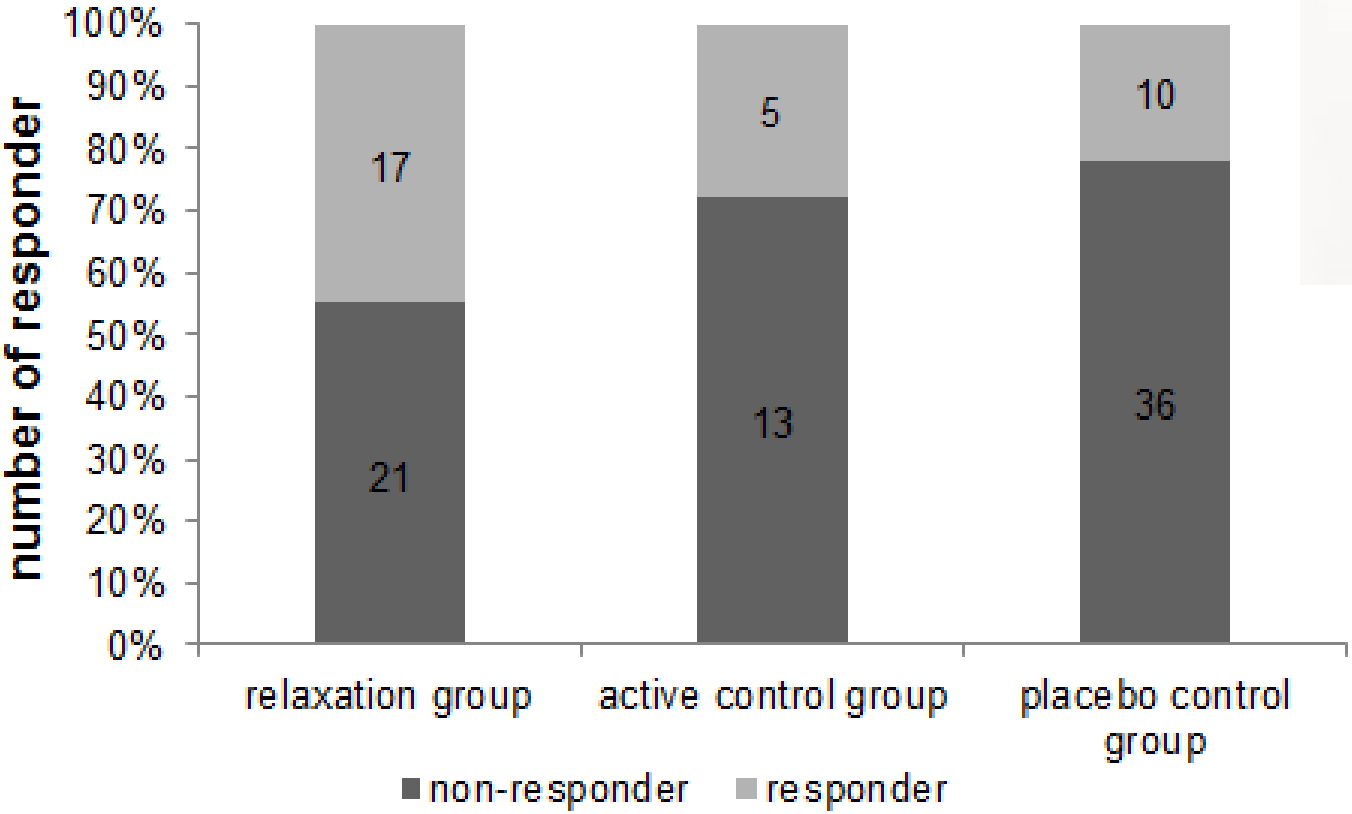
randomized

historical placebo control

Lehner et al., Sci Rep 2016

TMS + Entspannungstechnik
Pilotstudie



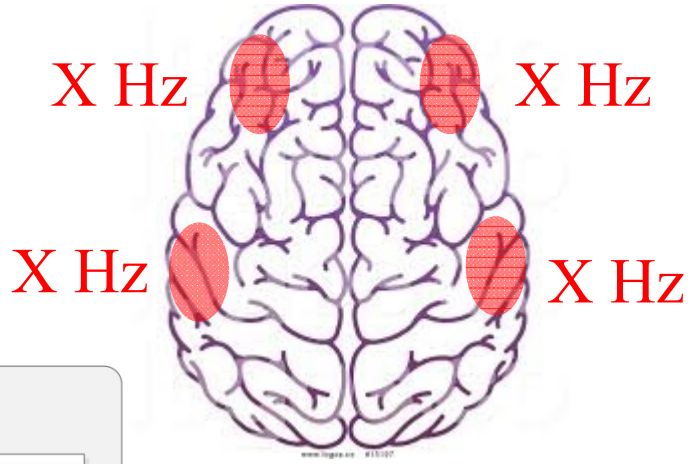


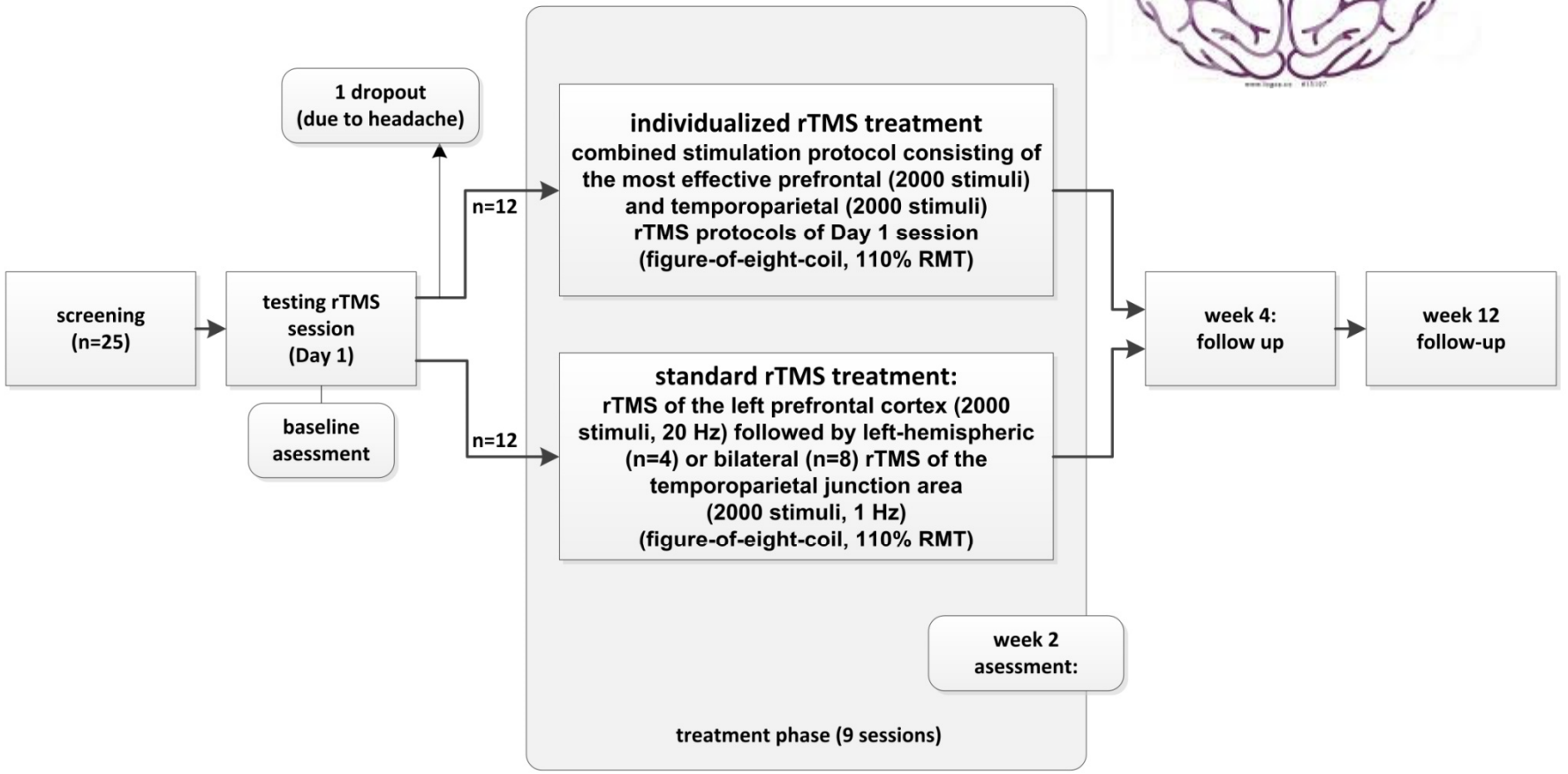
N = 38

Historische Kontroll-gruppen

Kreuzer et al., 2016

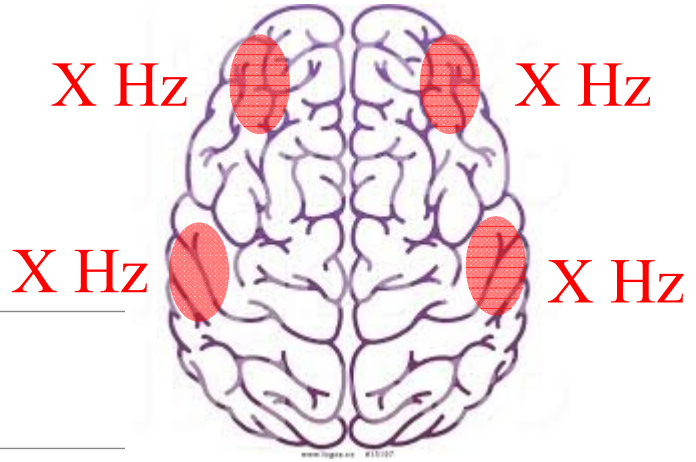
Individualisierte TMS Pilotstudie

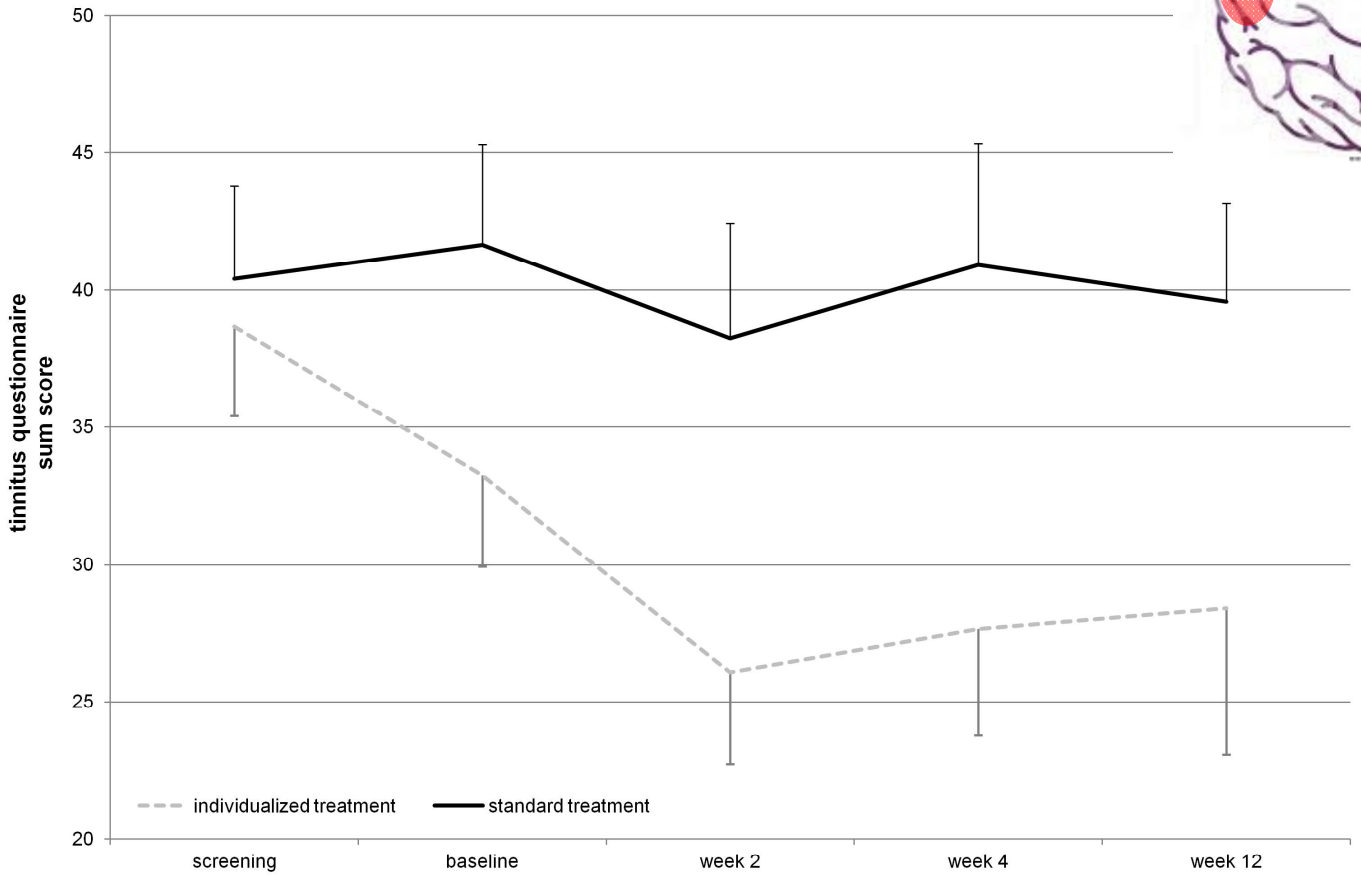




Kreuzer et al., submitted

Individualisierte TMS Pilotstudie





Kreuzer et al., submitted

Multimodale Stimuation

- Kombination von akustischer Stimulation mit TMS (priming, spike timing dependent plasticity)

  Speckmann et al. 2010

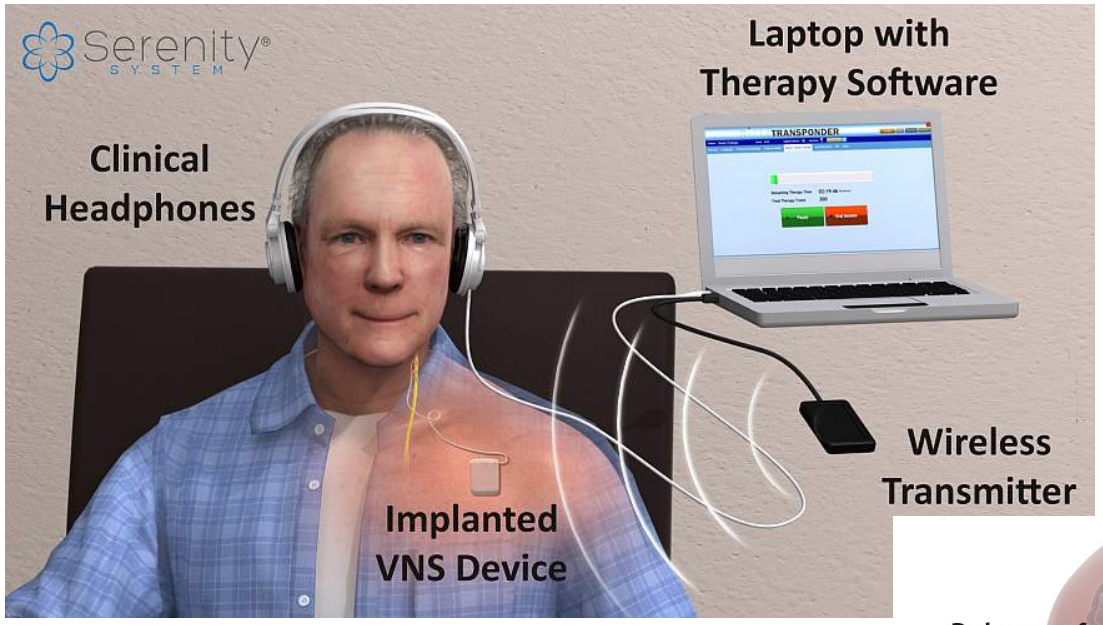
- Kombination von akustischer und somatosensorischer Stimulation

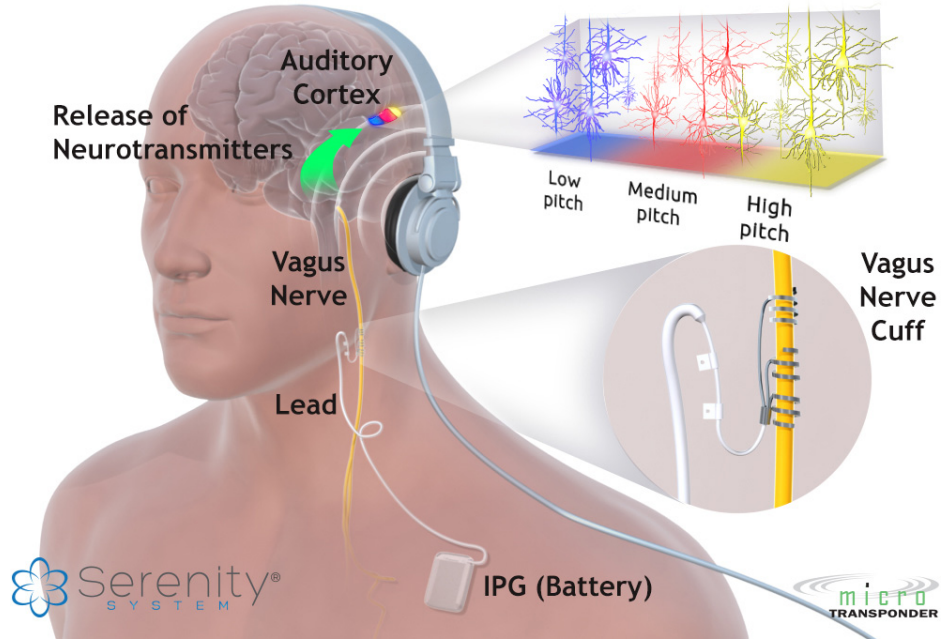
  Koehler et al. 2013; d'Arcy et al. 2017

- Gehirnstimulation zur Faziliterung der akustischen Stimulation

  Shekhawat et al. 2013, Teismann al. 2014, De Ridder et al. 2014

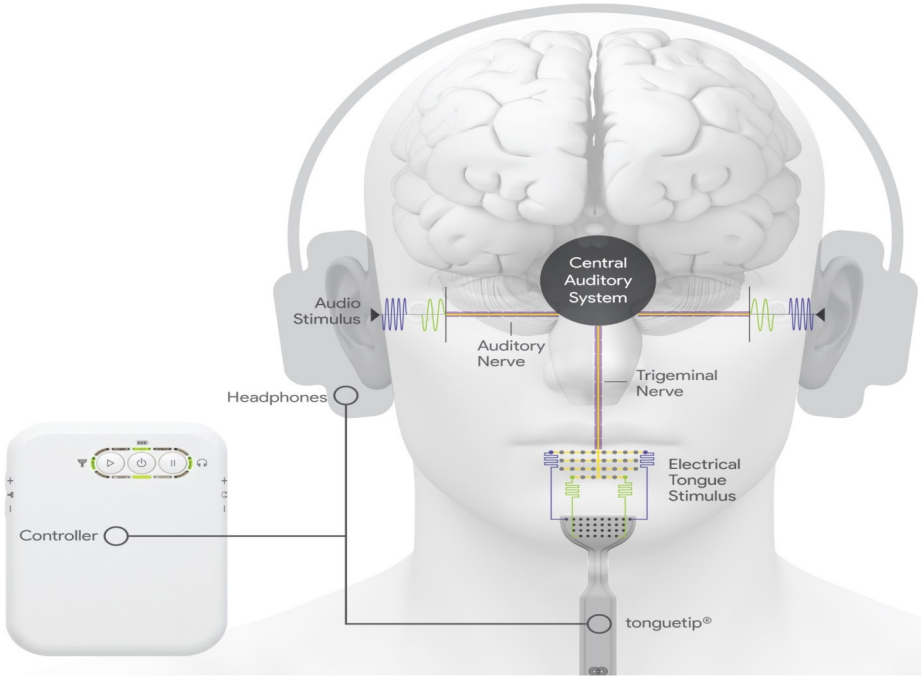
Vagusnervstimuation, gepaart mit auditorischer Stimulation

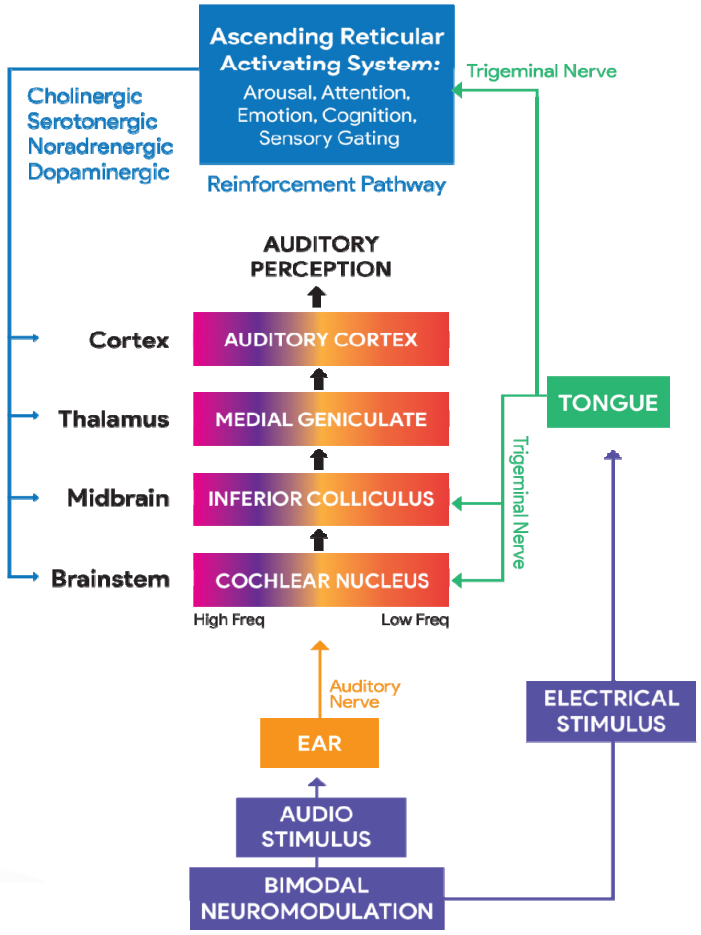




Bimodale Stimulation

Gerät zur bimodalen akustischen und sensorischen Stimulation

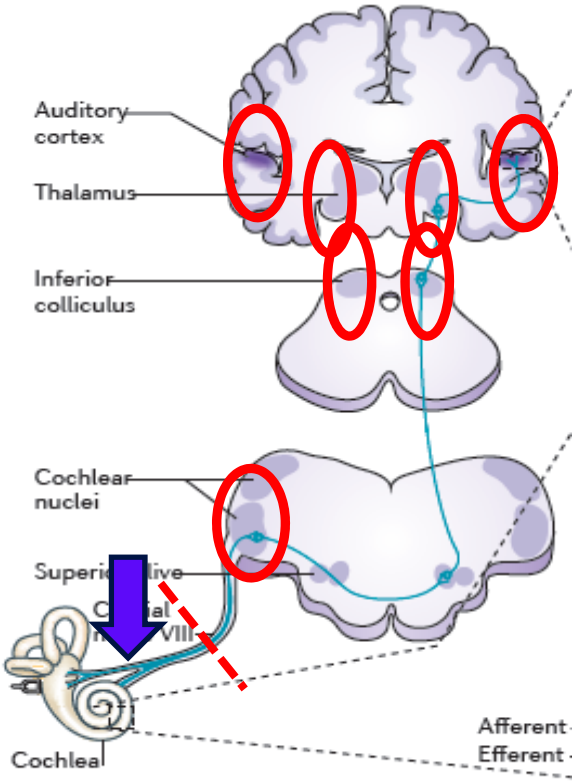


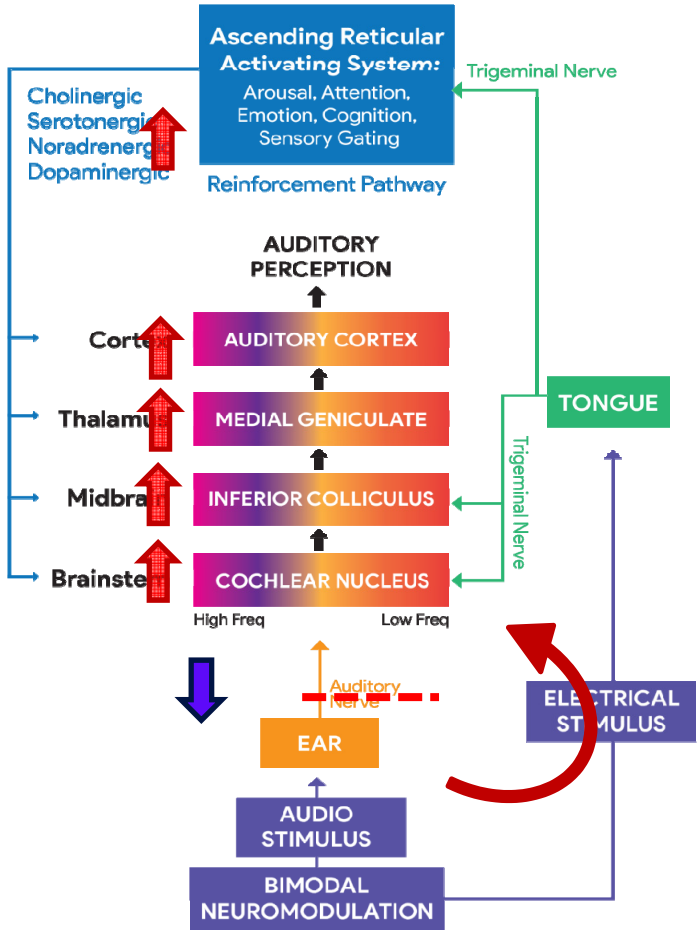


Hamilton et al. 2016; d'Arcy et al. 2017

Bimodale Stimulation

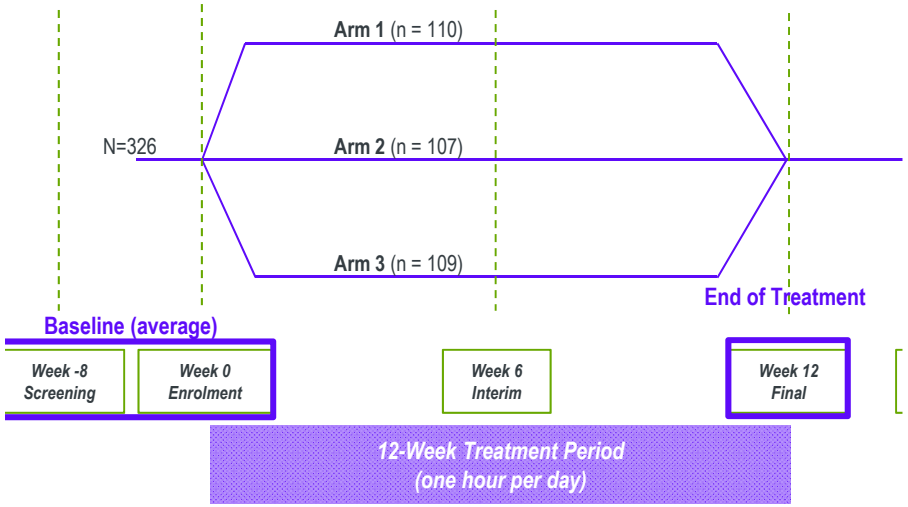
Wirkprinzip:

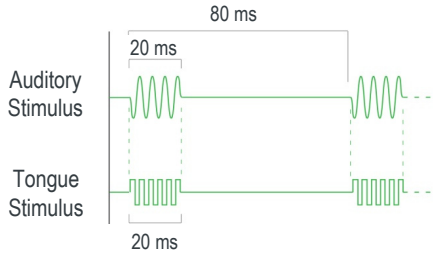


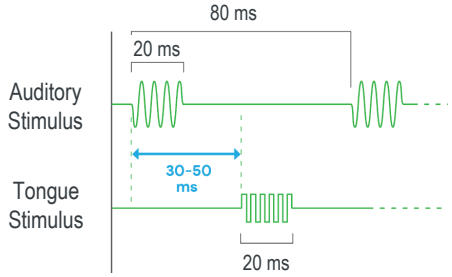


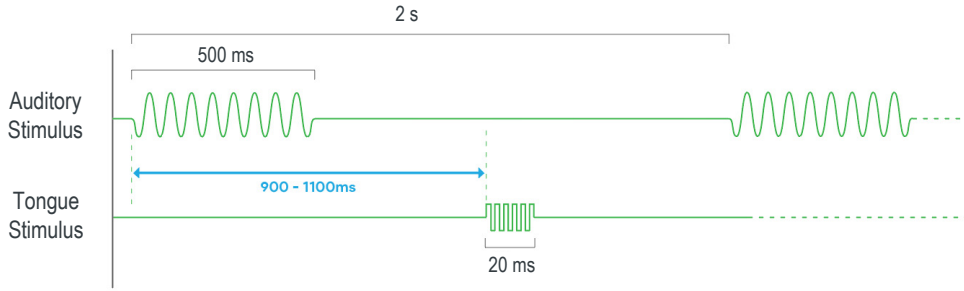
Hamilton et al. 2016; d'Arcy et al. 2017

Studiendesign

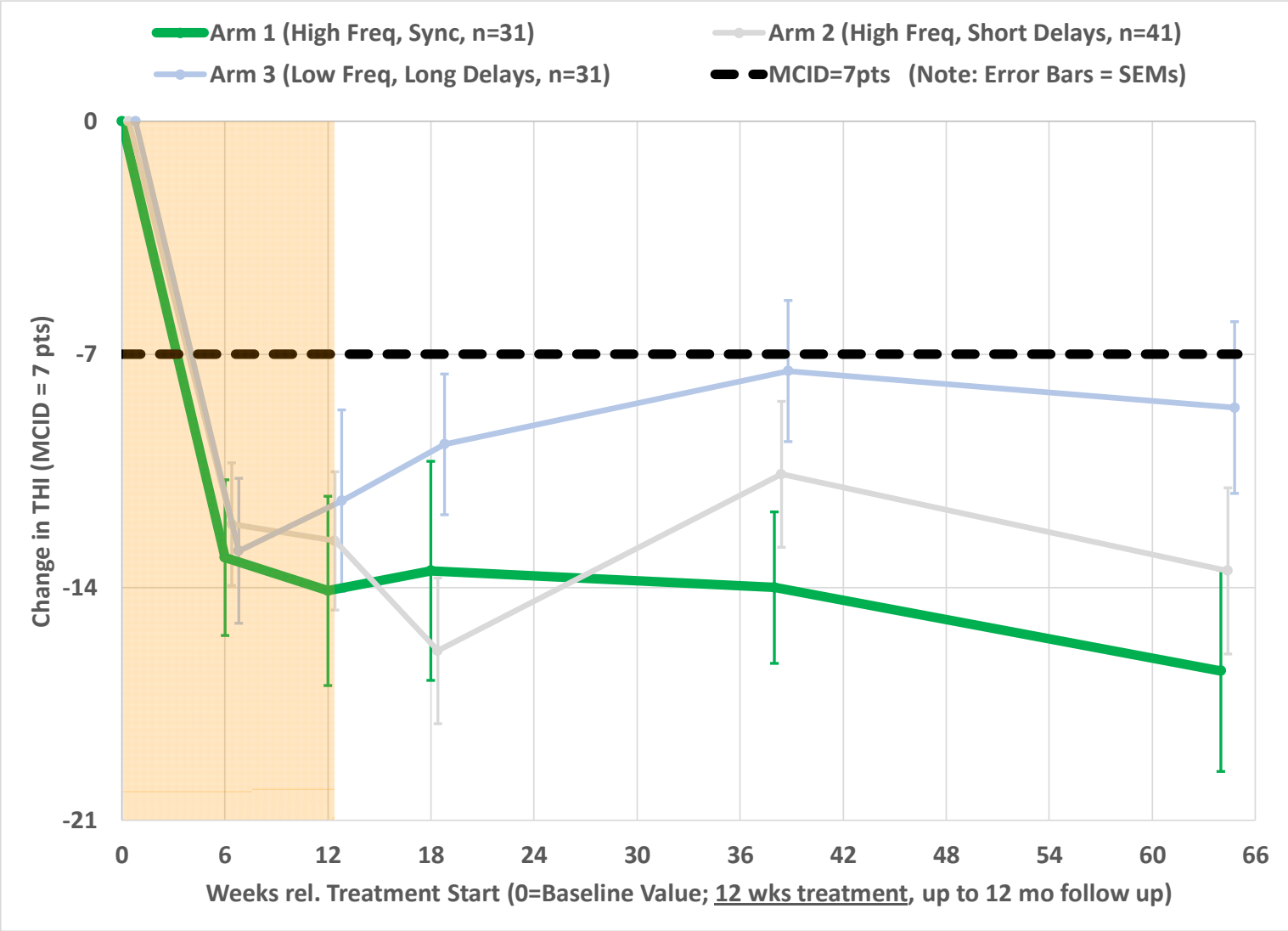








Ergebnisse


Arm 1 (High Freq, Sync, n=31)
Arm 2 (High Freq, Short Delays, n=41)
Arm 3 (Low Freq, Long Delays, n=31)
MCID=7pts (Note: Error Bars = SEMs)
Change in THI (MCID = 7 pts)
0
-7
-14
-21
0
6
12
18
24
30
36
42
48
54
60
66
Weeks rel. Treatment Start (0=Baseline Value; 12 wks treatment, up to 12 mo follow up)

Medikamentöse Therapie

ANNUAL REVIEWS

Annual Review of Pharmacology and Toxicology

Therapeutic Approaches to the Treatment of Tinnitus

Berthold Langguth,[1] Ana Belen Elgoyhen,[2,3] and Christopher R. Cederroth[4]

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[2]Instituto de Investigaciones en Ingeniería Genética y Biología Molecular "Dr. Héctor N. Torres," Consejo Nacional de Investigaciones Científicas y Técnicas, 1428 Buenos Aires, Argentina

[3]Instituto de Farmacología, Facultad de Medicina, Universidad de Buenos Aires, 1121 Buenos Aires, Argentina

[4]Department of Physiology and Pharmacology, Karolinska Institutet, 171 77 Stockholm, Sweden

Table 1 Effects of pharmaceutical treatment on chronic tinnitus

Drugs	Reference	Subjects	Type of study	Dosage	Results
Sodium channel blocker					
Lidocaine	Israel et al. (61)	26	Randomized placebo controlled	1–2 mg/kg of body weight intravenously for 3–4 min	Complete or partial tinnitus suppression in 19 out of 26 patients treated with IV lidocaine; no effect of IV saline
Antidepressants					
Amitryptiline	Bayar et al. (80)	37	Randomized placebo controlled	50–100 mg/day for 6 weeks	Decreased tinnitus intensity and subjective relief as compared to placebo
Nortriptyline	Sullivan et al. (78)	92	Randomized placebo controlled	50–150 mg/day for 6 weeks	Depression and tinnitus loudness decreased as compared to placebo
Paroxetine	Robinson et al. (83)	115	Randomized placebo controlled	Maximum of 50 mg/day for 100 days	No significant difference
Sertraline	Zoger et al. (82)	76	Randomized placebo controlled	25–50 mg/day for 16 weeks	Decreased loudness and severity as compared to placebo
Trimipramine	Mihail et al. (81)	19	Placebo controlled crossover	NA	No significant difference
Anticonvulsants					
Carbamazepine	Donaldson (163)	62	Randomized placebo controlled	100 mg/day	No significant difference
	Hulshof & Vermeij (95)	NA	Randomized placebo controlled	NA	No significant difference
Gabapentin	Bauer et al. (98)	39	Randomized placebo controlled	Maximum 2,400 mg/day for 20 weeks	Decrease in annoyance
	Witsell et al. (164)	76	Randomized placebo controlled	1,800 mg/day for 5 weeks	No significant difference
	Dehkordi et al. (99)	80	Randomized placebo controlled	NA	No significant difference
	Piccirillo et al. (100)	135	Randomized placebo controlled	900–3,600 mg/day for 8 weeks	No significant difference
Lamotrigine	Simpson et al. (101)	31	Randomized placebo controlled	25–100 mg/day for 8 weeks	No significant difference
Benzodiazepines/GABAergic drugs					
Alprazolam	Johnson et al. (87)	36	Randomized placebo controlled	0.25 or 0.5 mg/day for one week, increased to maximum of 1 mg/day for some patients for 56 days	Reduction in loudness as compared to placebo
	Jalali et al. (88)	36	Randomized placebo controlled	0.5 mg 1–3 times daily for 8 weeks	No significant difference
Baclofen	Westerberg et al. (117)	30	Randomized placebo controlled	Maximum 60 mg/day for 3 weeks	No significant difference
Clonazepam	Bahmad et al. (90)	30	Randomized placebo controlled	NA	Reduction of tinnitus annoyance and intensity (measured with a VAS) as compared to placebo
	Han et al. (91)	38	Open-label comparison to *G. biloba*	0.5 mg/day clonazepam and 4 mg/day *G. biloba*, increased from 1 to 4 doses daily for 5 weeks	Clonazepam more effective than *G. biloba*; tinnitus annoyance, duration, and loudness decreased
Diazepam	Kay et al. (89)	21	Placebo controlled crossover	NA	No significant difference
Glutamatergic drugs					
Acamprosate	de Azevedo et al. (107)	50	Randomized placebo controlled	333 mg three times daily for 3 months	Improvement over placebo
	Sharma et al. (108)	40	Randomized placebo controlled	333 mg TDS three times daily for 45 days	Significant improvement over placebo
Memantine	Figueiredo et al. (109)	43	Placebo controlled crossover	5–10 mg 1–2 times daily for 90 days	No significant difference
Neremexane	Suckfüll et al. (110)	320	Randomized placebo controlled	25–75 mg/day for 16 weeks	Decreased annoyance and impact on life at higher dosage
Others					
Atorvastatin	Olzowy et al. (122)	50 (ages between 60 and 75)	Randomized placebo controlled	40 mg/day for 13 months	Trend toward relief from tinnitus without reaching statistical significance
Betahistine	Sonmez et al. (124)	68	Randomized placebo controlled	48 mg/day for 3 months	Slight improvement in loudness and on THI
Cilostazol	Lim et al. (135)	50	Randomized placebo controlled	200 mg/day for 4 weeks	Statistically significant difference between cilostazol and placebo in the VAS score but not in the THI
Cyclandelate	Hester et al. (125)	59	Randomized placebo controlled	Cyclandelate for 3 months	No significant difference
Deanxit	Meeus et al. (126)	28	Placebo controlled crossover	1 mg/day for 3 weeks added on to clonazepam	Reported tinnitus improvement in 3 out of 28 subjects
G. biloba	Hilton et al. (22)	1,543	Cochrane meta-analysis	NA	No significant difference
Melatonin	Rosenberg et al. (165)	30	Placebo controlled crossover	3 mg/day for 30 days	No significant difference for the whole group; tendency toward a beneficial effect in patients with tinnitus and insomnia
	Hurtuk et al. (129)	61	Placebo controlled crossover	3 mg/day for 30 days	Statistically significant decrease in tinnitus intensity and improved sleep quality
Misoprostol	Yilmaz et al. (133)	40	Randomized placebo controlled	Treatment at increasing dosage for 4 months	Statistically significant difference between misoprostol and placebo in tinnitus loudness, but not in subjective tinnitus scoring
Odansetron	Taslimi et al. (132)	60	Randomized placebo controlled	16 mg/day for 4 weeks	Statistically significant difference between odansetron and placebo in the Tinnitus Severity Index score but not in the VAS score and THI
Oxytocin	Azevedo et al. (130)	16	Placebo controlled crossover	Single dose of 16 IU oxytocin	Statistically significant difference between oxytocin and placebo in the CGI score but not in the VAS score
Piribedil	de Azevedo et al. (114)	56	Randomized placebo controlled	50 mg/day for 90 days	No difference from placebo
Pramipexole	Sziklai et al. (115)	40	Randomized placebo controlled	Maximum dosage 0.7 mg three times daily for 4 weeks	35% of pramipexole group improved in tinnitus annoyance
Vardenafil	Mazurek et al. (136)	42	Randomized placebo controlled	20 mg/day for 12 weeks	No significant difference
Vitamin B12	Berkiten et al. (139)	83 patients with vitamin B12 deficiency	Randomized placebo controlled	1 g/mL injected daily for 5 days, then once a month for 12 months	No significant difference
	Singh et al. (138)	40	Randomized placebo controlled	2,500 μg weekly for 6 weeks	Significant improvement in patients with vitamin B 12 deficiency
Zinc	Person et al. (140)	209	Cochrane meta-analysis	Zinc supplementation	No significant difference

Abbreviations: CGI, Clinical Global Impressions; IV, intravenous; NA, not available; TDS, total dissolved solids; THI, Tinnitus Handicap Inventory; VAS, Visual Analogue Scale.

Medikamentöse Therapie

Keine replizierten positiven Daten von randomisierten kontrollierten Studien

Kein Medikament zur Behandlung des Tinnitus zugelassen

Mehrere Entwicklungsprogramme für innovative Ansätze waren nicht erfolgreich (Esketamin intraaurikulär, Kaliumkanalmodulatoren, AMPA Antagonisten)

Seltene Sonderformen von Tinnitus können wirkungsvoll behandelt werden (Typewriter-Tinnitus: Carbamazepin, endolymphatischer Hydrops: Betahistin)

Häufige Begleiterkrankungen wie Schlafstörungen, Angststörungen und Depressionen können wirksam medikamentös behandelt werden

Medikation for Komorbiditäten

Depression

- S-Citalopram 10 mg
- Sertralin 50-100 mg

Insomnie

- Trimipramin 25-50 mg
- Mirtazapin 7.5-15 mg
- Pregabalin 25-100 mg

Angst

- Opipramol 50mg
- Pregabalin 150-300 mg

Intermittierende Tinnitus”bursts”

- Carbamazepin 150-600 mg
- Lamotrigin 100-200 mg

Investigated drug targets for pharmacologic treatment

- **NMDA:** Caroverine (topical / systemic): inconclusive results (Ehrenberge et al.)
- Acamprosate (systemic): positive (Azevedo et al. 2007, Sharma et al. 2012)
- Memantine (systemic): negative (Figueiredo et al. 2008)
- Neramexane (systemic): negative (Suckfüll et al. 2011)
- *Merz*
- Gacyclidine (topical): only pilot data (Wenzel et al. 2010
- *Ipsen, Neurosystec. Otonomy*
- S-Ketamine (topical): inconclusive results (van de Heyning et al. 2014)
- *Auris Medical*
- **AMPA:** BGG492 (systemic): no results published
- *Novartis*

Investigated drug targets for pharmacologic treatment

- **GABA:** Clonazepam — positive (Han et al. 2012)
- Alprazolam — positive (Jalali et al. 2009)

- **Dopamin:** Piribedil (systemic): — negative (Azevedo et al.. 2009)
- Pramipexol (systemic): — positive (Sziklai et al. 2011)
- Sulpiride (systemic) — inconclusive (Lopez-Gonzales et al. 2003)

- **Serotonin:** Sertralin (systemic): — negative (Zöger et al. 2006)
- Nortriptylin (systemic): — negative (Sullivan et al. 1993)

- **Potassium channel modulators:**
- **Kv7:** Flupirtin (systemic) — negative (De Ridder et al. 1996)
- Retigabine (systemic) — ???
- **Kv3: AUT 000063 (systemic)** — **negative (data not yet published)**
- ***Autifony***

Negative results

- **Anticonvulsants** — Cochrane Meta-Analysis (Hoekstra et al. 2011)
- **Antidepressants** — Cochrane Meta-Analysis (Baldo et al. 2012)
- **Gingko** — Cochrane Meta-Analysis (Roland and Nergard 2012)
- **Zinc** — (Coelho et al. 2013)
- **Atorvastatin** — (Olzowy et al. 2007)
- **Vardenafil** — (Mazurek et al. 2009)
- **Melatonin** — (Miroddi et al. 2015)

Selbstmanagement

https://www.trackyourtinnitus.org/

Ecological Momentary Assessment

https://www.trackyourtinnitus.org/

frontiers in Aging Neuroscience

METHODS
published: 15 December 2016
doi: 10.3389/fnagi.2016.00294

Measuring the Moment-to-Moment Variability of Tinnitus: The TrackYourTinnitus Smart Phone App

Winfried Schlee[1], Rüdiger C. Pryss[2], Thomas Probst[3,4], Johannes Schobel[2], Alexander Bachmaier[2], Manfred Reichert[2] and Berthold Langguth[1]*

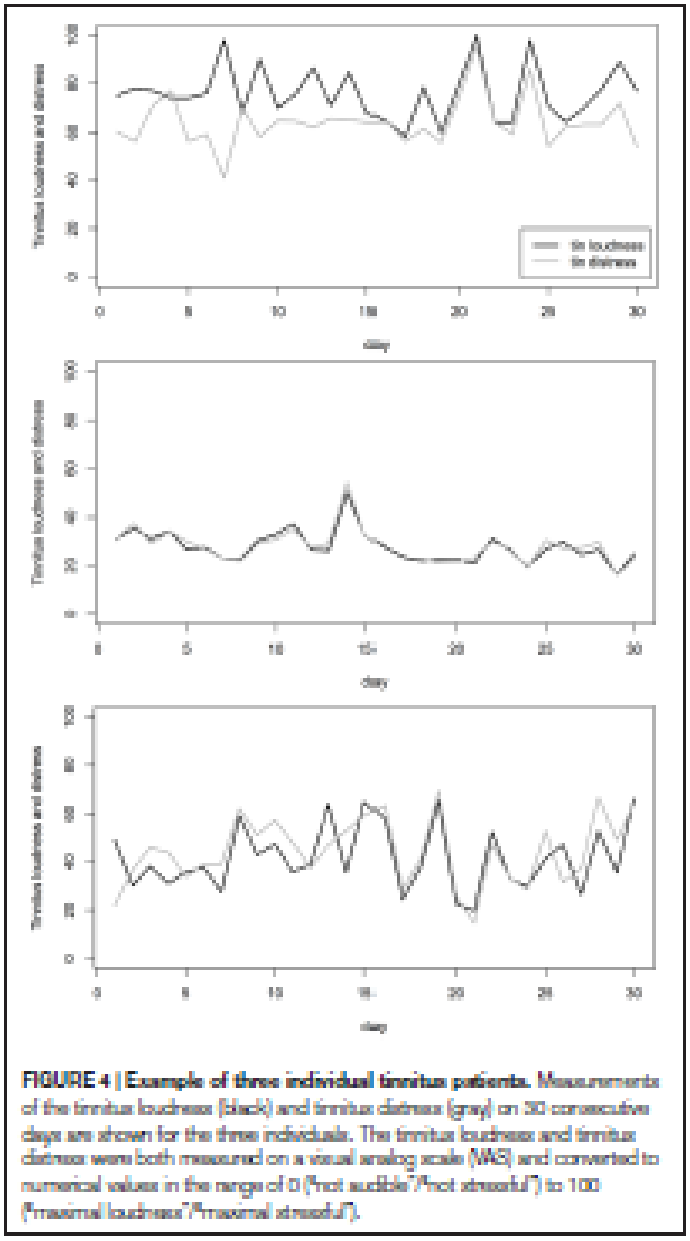

FIGURE 4 | Example of three individual tinnitus patients. Measurements of the tinnitus loudness (black) and tinnitus distress (gray) on 30 consecutive days are shown for the three individuals. The tinnitus loudness and tinnitus distress were both measured on a visual analog scale (VAS) and converted to numerical values in the range of 0 ("not audible"/"not stressful") to 100 ("maximal loudness"/"maximal stressful").

Schlee et al. Front Ageing Neurosci 2017

frontiers in Aging Neuroscience

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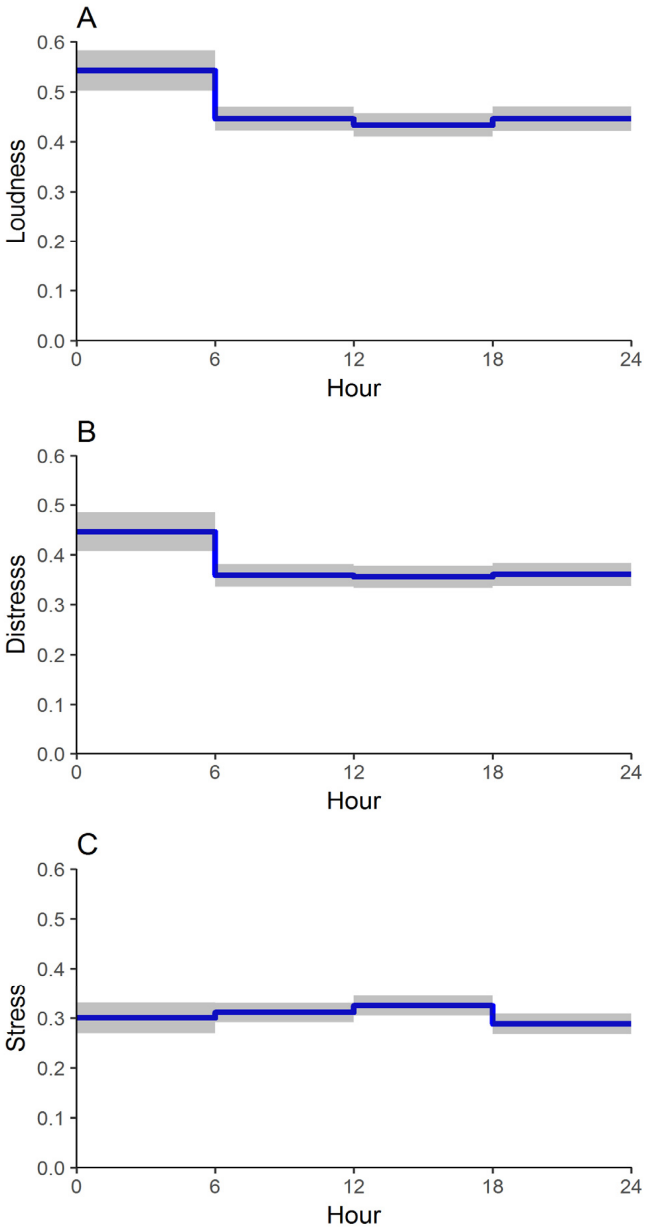
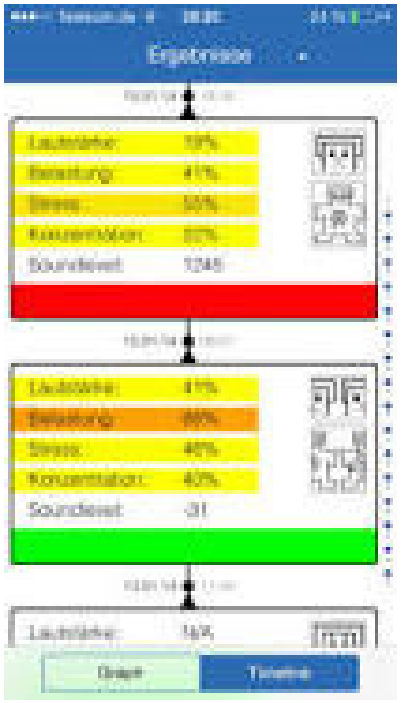
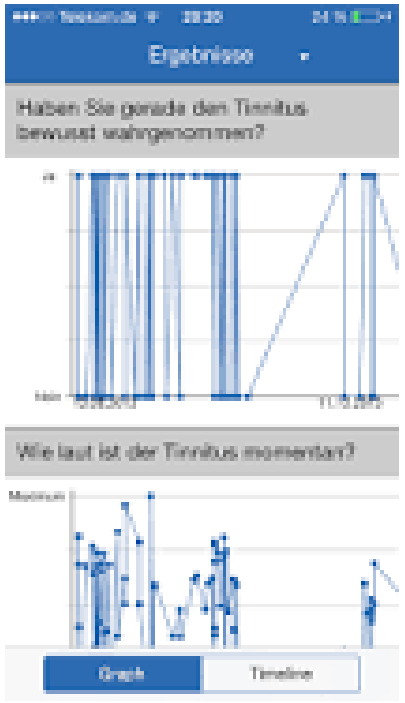


Probst et al. Front Ageing Neurosci 2018

assessment

feedback





Zusammenfassung

Der multidisziplinären Diagnostik und Therapie kommt eine entscheidende Bedeutung zu.

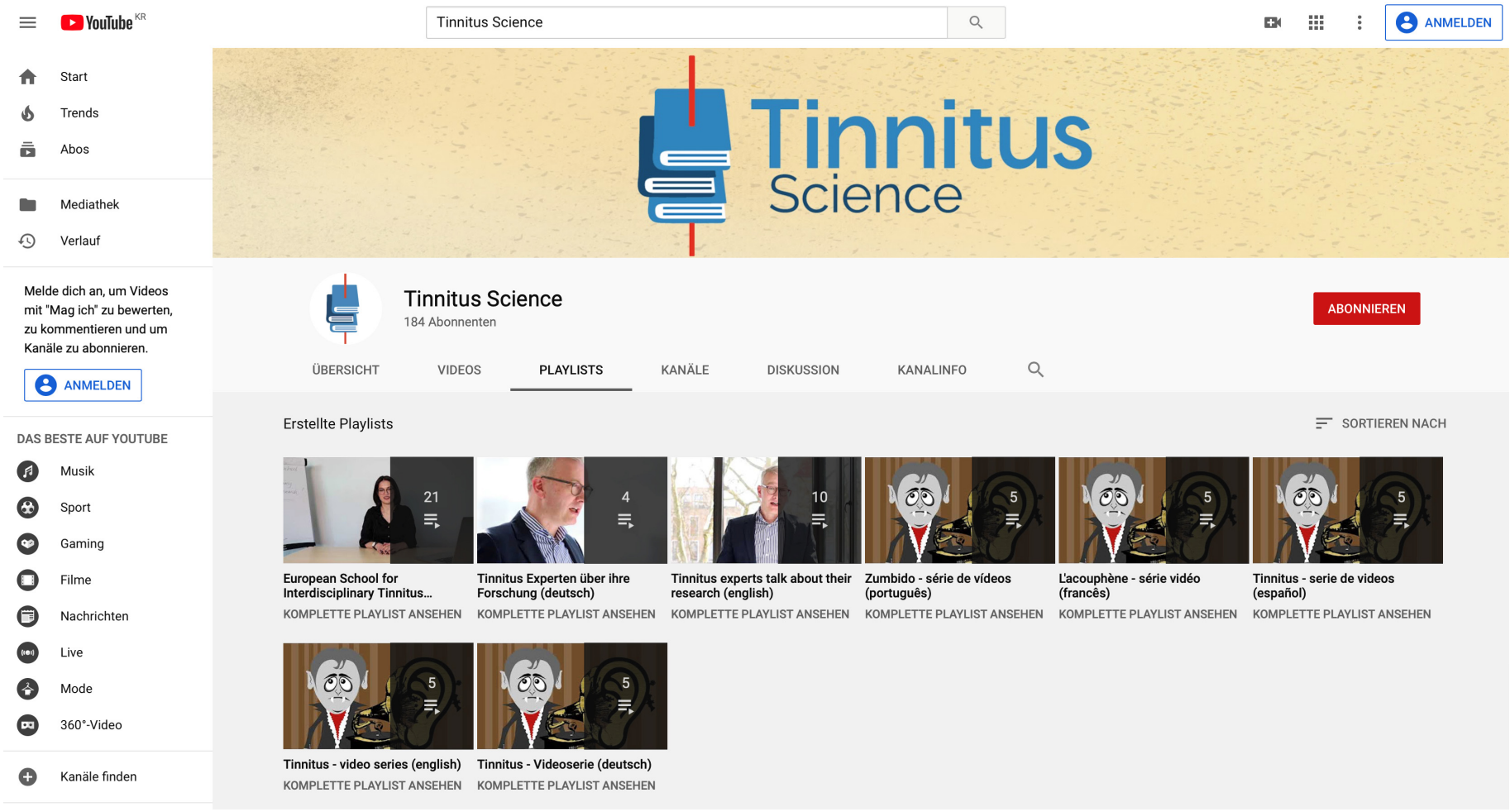
Verfügbare Behandlungsmöglichkeiten umfassen das beratende therapeutische Gespräch, kognitive Verhaltenstherapie sowie verschiedene Formen akustischer Stimulation.

Neuromodulatorische Techniken und medikamentöse Therapien befinden sich in Entwicklung.

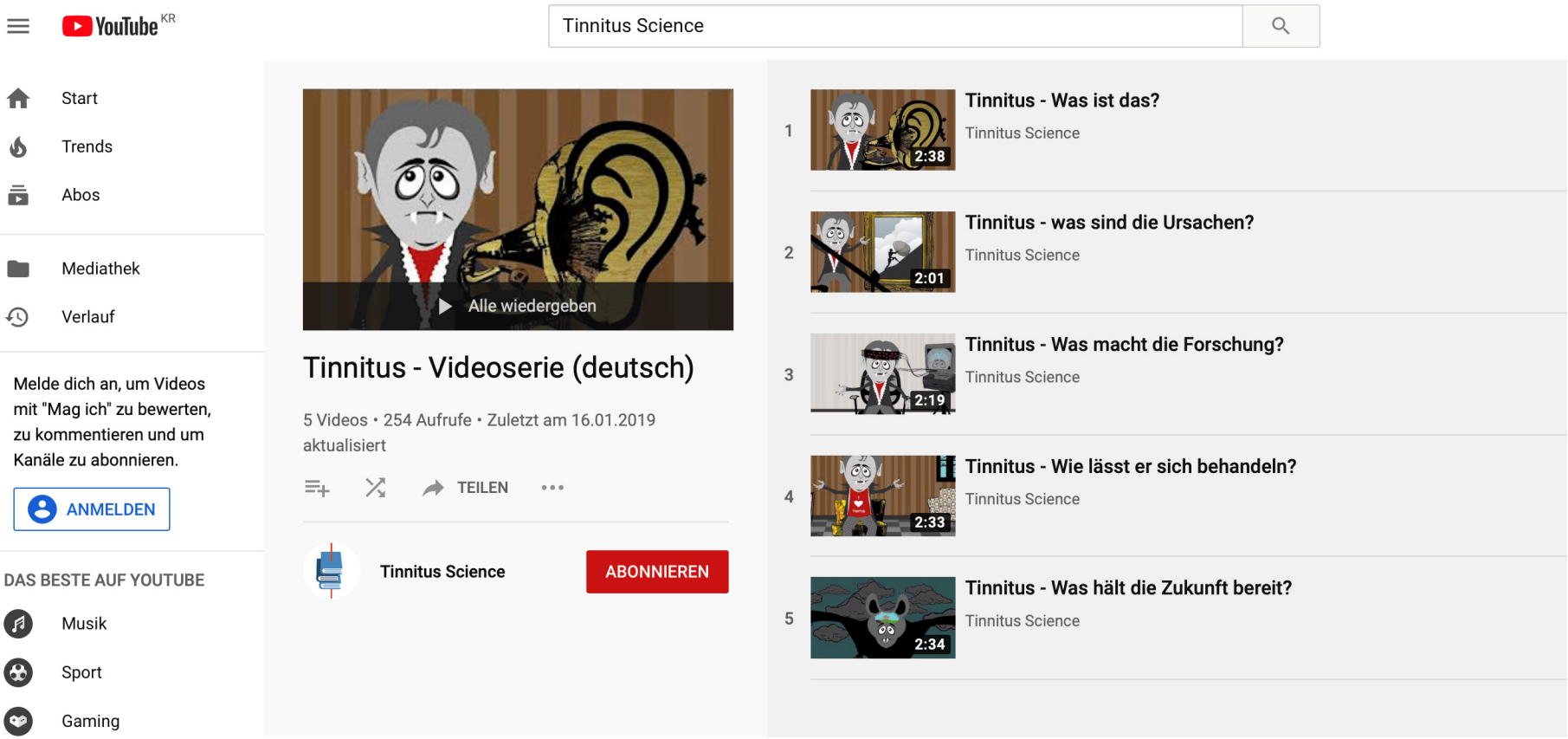
Die Indikation zur pharmakologischen Behandlung beschränkt sich derzeit auf spezifische Tinnitussubtypen sowie die Behandlung komorbider Depressivität, Schlaf- und Angststörungen.

Besonders für schwer betroffene Tinnituspatienten ist es wichtig, im behandelnden Arzt einen verlässlichen Ansprechpartner zu haben.

Youtube: Tinnitus Science



Youtube: Tinnitus Science



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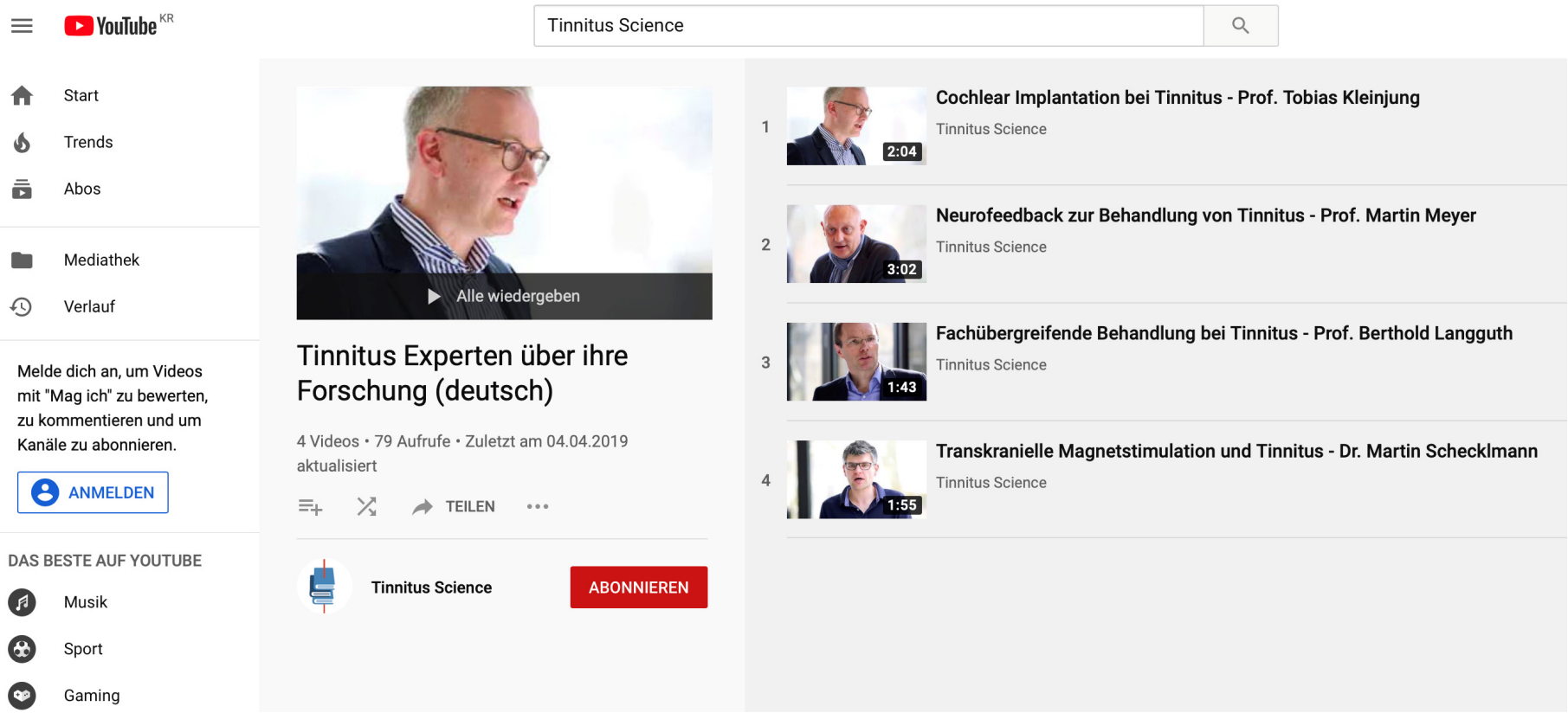


Gut daß ich
heute trotz
meines Tinnitus
gut schlafen
kann