Tinnitus and Influencing Comorbidities

\odot \odot \odot =



Authors

Birgit Mazurek¹, Benjamin Boecking¹, Christian Dobel², Matthias Rose³, Petra Brüggemann¹

Affiliations

- 1 Tinnitus Center, Charité Universitätsmedizin Berlin, Berlin, Germany
- 2 Department of Oto-Rhino-Laryngology, University Medicine of Jena, Jena, Germany
- 3 Department of Psychosomatic Medicine, Charité Universitätsmedizin Berlin, Berlin, Germany

Key words

Tinnitus, comorbidity, depression, anxiety, pain, cognition

Bibliography

Laryngo-Rhino-Otol 2023; 102: S50–S58

DOI 10.1055/a-1950-6149

ISSN 0935-8943

© 2023. The Author(s).

This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commecial purposes, or adapted, remixed, transformed or built upon. (https://creativecommons.org/licenses/by-nc-nd/4.0/)

Georg Thieme Verlag, Rüdigerstraße 14, 70469 Stuttgart, Germany

Correspondence

Prof. Dr. Birgit Mazurek Tinnitus Center, Charité – Universitätsmedizin Berlin Charitéplatz 1 10117 Berlin Germany birgit.mazurek@charite.de

ABSTRACT

Numerous studies show that impairments in chronic tinnitus are closely connected with psychosomatic and other concomitant symptoms. This overview summarizes some of these studies. Beyond hearing loss, individual interactions of medical and psychosocial stress factors as well as resources are of central importance. Tinnitus related distress reflects a large number of intercorrelated, psychosomatic influences - such as personality traits, stress reactivity and depression or anxiety - which can be accompanied by cognitive difficulties and should be conceptualized and assessed within a vulnerabilitystress-reaction model. Superordinate factors such as age, gender or education level can increase vulnerability to stress. Therefore, diagnosis and therapy of chronic tinnitus be individualised, multidimensional and interdisciplinary. Multimodal psychosomatic therapy approaches aim to address individually constellated medical, audiological and psychological influences in order to sustainably increase the quality of life of those affected. Counselling in the first contact is also indispensable for diagnosis and therapy.

Contents

	Abstract	S50
1.	Introduction	S51
2.	Multidimensional character of tinnitus	S51
3.	Interplay of neuronal networks of the tinnitus experience	S52
4.	Comorbidities and influencing factors	S52
4.1	Depression, anxiety, and stress	S52

4.2	Subjective pain experiences	S53
4.3	Hearing loss	S53
4.4	Cognitive influences	S54
5.	Treatment options	S54
6.	Conclusion and outlook	S54
	References	S55

1. Introduction

Subjective tinnitus is defined as the "conscious awareness of a tonal or composite noise for which there is no identifiable corresponding external acoustic source" which can be "associated with emotional distress, cognitive dysfunction, and/or autonomic arousal leading to behavioral changes and functional disability" [1].

How the tinnitus symptom impacts upon patients' daily lives is complex and largely determined by associated psychological experiences [2]. For example, it is crucial to distinguish between the "tinnitus sound" as an initial tonal symptom and "tinnitus-related distress" as a multi-layered psychological phenomenon. Current research suggests that reactive tinnitus-related distress is particularly important – as it can significantly facilitate chronification of the often harmless initial symptomatology [2, 3]. Tinnitus-related distress emerges against a background of pre-existing medical, psychological or social vulnerability and can manifest itself in a variety of functional phenomena, such as (1) other functional hearing disorders (e. g. hyperacusis), or (2) anxiety and depression cycles, which, in turn may involve (a) sleep or concentration difficulties, (b) cognitive difficulties, or (c) mood volatility [4].

Tinnitus is a common symptom: at least 14,7% of the European population are affected at some point in their lives – and about one in a hundred people (1,2%) reports high emotional distress following its onset [5]. The prevalence of tinnitus significantly increases with age and a deterioration of hearing ability [5]. Worldwide, the treatment of tinnitus causes significant cost, in particular when the symptom is experienced as highly distressing [6,7].

Often – yet not always [8] – hearing loss or a hearing-related disorder precedes the emergence of the tinnitus sound [9–11]. Other risk factors include neurological (e. g. meningitis), cardiovascular (e. g. hypertension), or metabolic influences (e. g. diabetes mellitus) [12, 13]. Irrespective of potential medical influences, however, tinnitus-related distress has to be understood as a reflection of psychological experience that either reflects pre-existing emotional distress or distress as triggered by the tinnitus sound stimulus [14, 15]. Emotional distress can precede sudden hearing loss [16], facilitate the chronification of tinnitus perception[17], increase muscle tension [18] or, conversely, be triggered or intensified by the tinnitus sound [19, 20]. Interactions between the often harmless tinnitus sound and tinnitus-related distress are crucial for multimodal conceptualization and treatment of chronic tinnitus.

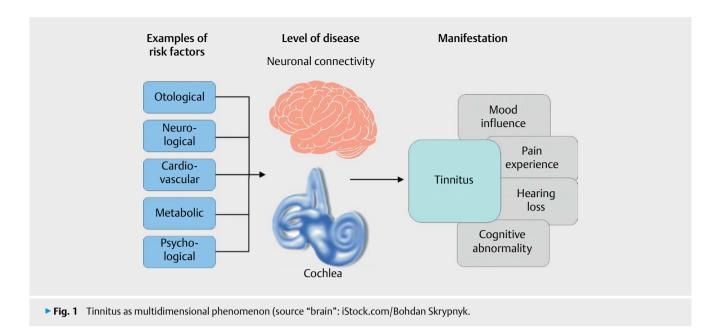
2. Multidimensional character of tinnitus

The current practice of diagnosing isolated index problems and categorically conceptualized 'comorbid' conditions, based on classification systems such as the DSM and ICD, is a hindrance to understanding multidimensional problems and developing effective treatment strategies. Tinnitus-related distress reflects many dimensional, interdependently connected influencing factors: Whilst the tinnitus *sound* can originate from medical risk factors such as hearing loss or vascular conspicuities [12], tinnitus-related *distress* and chronification is caused and maintained by psychological influences that must be individually and holistically formulated within a vulnerability-stress-reaction model [19, 21, 22]. Consequently, therapeutic approaches must be interdisciplinarily conceptualized [23, 24]. In this context, it is particularly relevant to turn to intensified psychosomatic diagnostics and treatment, including psychological vulnerability and concormitant factors – focusing on individual psychological and psychosomatic vulnerability, stress and coping factors [18] (**> Fig. 1**).

In a recently published study, Brueggemann et al. [25] demonstrated that tinnitus-related distress was closely associated with depressive experiences, emotional distress and other somatisation tendencies. These associations were more pronounced in people of older age and lower education – general risk factors for psychological distress [26]. While patients often attribute their emotional distress to the tinnitus symptom, pre-existing psychological distress likely extends towards the tinnitus sound as being experienced as more threatening [27]. The tinnitus sound itself can further be experienced as emotionally distressing –often in the context of preexisting psychological vulnerability [19, 21, 28].

One study of tinnitus patients [21] used the revised Freiburg Personality Inventory (FPI-r) alongside a measure of perceived stress and demonstrated that tinnitus-related distress resulted from individual interactions of psychological vulnerability as reflected in measured personality traits and subjective stress experiences. The authors showed that certain personality traits (e.g. emotional excitability or inhibited aggressivity) interacted with perceived stress experiences in the here-and-now in explaining tinnitus-related distress. The study's particular relevance lies in its emphasis of individual psychological interactions and the importance of thereon-based treatment strategies [21]. A follow-up study demonstrated that psychosomatic and psychotherapeutic treatment of subjective stress experiences and worry lastingly reduced tinnitus-related distress [29]. > Fig. 2 (a) illustrates the vulnerability-stress-reaction model and (b) putative psychosomatic associations in chronic tinnitus.

People with chronic tinnitus have a heterogeneous profile and often a complex medical history [30]. To reduce this heterogeneity, a recently published study [31] identified four subgroups of tinnitus patients ("phenotypes"): The first group is characterized by emotional avoidance tendencies and comprised a large proportion of the study sample. Apart from the index symptom "chronic tinnitus", members of this group reported little psychological distress - yet sought treatment in a psychosomatic treatment setting. The authors suggested that, in this group, the tinnitus symptom might be understood as a somatisation phenomenon that occurs within a broader context of emotional avoidance tendencies [32]. The second group comprised 15% of the study sample and patients reported high psychosomatic burden, as reflected in high levels of tinnitus-related distress, depression, and anxiety alongside low psychological coping abilities such as self-efficacy or optimism and low quality of life. In this group, depressive or anxious symptoms are seen as the basis of the general symptom burden and tinnitus can be placed in a broader context of psychological stress experience. This subgroup included proportionally more women and patients who tended to live alone, seek work, or be less formally qualified. The third group was characterized by physical tension and subjective pain experiences that were highly correlated with emotionaland tinnitus-related distress. The fourth group was characterized by patients that showed strong associations between the tinnitus symptom and high levels of psychological stress - including anxious-depressive mood and related feelings of fatigue or exhaustion



respectively. Members of this group included proportionally more men and tended to be younger and employed. Overall, the study emphasized the importance of emotional distress (and its avoidance) in the maintenance of tinnitus-related distress. Physiological or genetic correlates of these distress experiences are the subject of ongoing psychosomatic research [33–38].

3. Interplay of neuronal networks of the tinnitus experience

It is currently assumed that chronic tinnitus is represented in "central" neural networks [39]. Different neurophysiological approaches that investigate the genesis of the tinnitus sound feature tonotopic reorganisation, neuronal synchronicity, neuronal spontaneous activity, or the limbic processing of auditory information [40, 41]. In addition to auditory cortical regions, extra-auditory areas such as the limbic system (insula and amygdala), the anterior gyrus cinguli, the ventral striatum, and the prefrontal cortex appear to be involved in chronic tinnitus symptomatology [42, 43]. Individuals with hearing loss also show neurophysiological changes in the firing rate of neurons along the central auditory pathway, neuronal synchronicity, and tonotopic organisation. These changes may reflect neuroplastic processes that can also occur as a result of the prolonged attentional focusing of the tinnitus sound [44]. In addition, compared to healthy subjects, patients with chronic tinnitus showed neurophysiological differences in the processing of affectively significant auditory stimuli in the area of the orbitofrontal brain and limbic system [45].

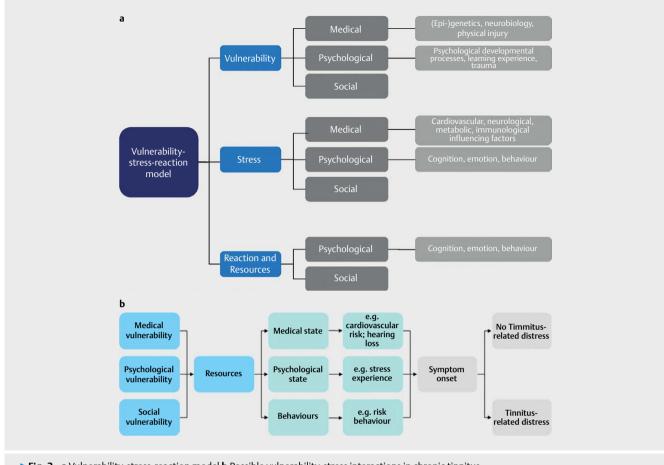
De Ridder et al. [42] describe a working model in which a conscious perception of the tinnitus sound results from increased neuronal activity of the sensory cortex. Herein, the tinnitus sound is considered as salient by means of parallel activated neuronal (self-) attention networks, and is evaluated affectively within a frontallimbic non-specific distress network (anterior cingulate cortex, anterior insula and amygdala). By means of classical and operant conditioning processes, a coupling of conscious perception of the "tinnitus sound" and "distress experience" occurs both neurophysiologically and psychologically.

4. Comorbidities and influencing factors

Chronic tinnitus can be associated with severe distress. Studies using a categorical comorbidity model report that a large proportion of individuals with chronic tinnitus suffer from 'comorbid disorders'. In particular, anxiety disorders and depression [46–53] are common, as are other somatoform disorders [4, 54]. Studies examining subordinate phenomena further report strong associations between tinnitus-related distress and symptoms such as sleep [55] or concentration [56] difficulties.

4.1 Depression, anxiety, and stress

It appears that tinnitus-related distress is most closely interlinked with depressivity - also owed to strong construct overlap and similarities in psychological stimulus processing [57]. Emotional distress experiences as reflected in anxiety, depressivity or emotional exhaustion alongside associated symptoms such as sleep disturbances are often already present at the time of tinnitus onset. Thus, they are considered crucial for the chronification of the tinnitus sound [2, 3, 18]. Physical and emotional exhaustion can facilitate an increased perception of the tinnitus sound thereby negatively influencing its processing and experience [2]. Due to mutual reinforcement of these factors, the tinnitus sound is the "catalyst" of a vicious cycle between pre-existing vulnerability or reactive emotional experience and perception of the tinnitus sound. For example, one study demonstrated that 52,2 % of a sample of 1490 patients with chronic tinnitus reported depression [58]. Understanding the interaction and construct overlap of tinnitus-related distress and depressivity may improve prevention, assessment, conceptualization and treatment of both symptom groups [29, 59].



▶ Fig. 2 a Vulnerability-stress-reaction model b Possible vulnerability-stress interactions in chronic tinnitus

Studies also show a close relationship between stress and tinnitus-related distress [60, 61]. Whilst cause-effect relationships remain unclear as well, chronic stress, which closely resembles anxiety and depression in its physiological effects [62] may reflect an increased vulnerability to tinnitus onset and tinnitus-related distress [63].

4.2 Subjective pain experiences

One strand of research examines similarities between chronic tinnitus and chronic pain experiences, as some chronic tinnitus patients describe co-occurrence of the tinnitus-related distress and pain sensations such as ear-, or headaches [64]. Paralleling models of chronic pain development and maintenance [65, 66], chronification of the tinnitus percept may be related to altered signal processing in the central nervous system alongside closely linked accompanying psychological factors [67]. In particular, interactions between the limbic system and the auditory or somatosensory cortex may play a role to this regard [42, 68]. A recent study investigated the co-occurrence of tinnitus-related distress and affective pain experiences [69]. Both symptom clusters were shaped by psychological factors such as depressiveness, perceived stress experiences, and coping attitudes – the therapeutic addressing of which was able to improve both symptom groups [29].

4.3 Hearing loss

In acoustic processing, sound signals are converted into afferent activity of the auditory nerve, which increases the activity of hierarchically ascending neural networks [70]. The acoustic signal travels through the brainstem, midbrain, and thalamic nuclei to the auditory cortex where it is given meaning by the non-auditory salience network and is consciously perceived [70]. At the same time, connections between the salience network and the limbic system assign emotional meaning to the sound [71].

Medically, hearing loss can often precede the onset of the tinnitus sound [72], and neurophysiological models discuss the effects of hearing loss on the auditory system, from the cochlea to the auditory cortex [73–75]. Hearing loss is often, but not always, associated with chronic tinnitus symptomatology [12, 76, 77] and has sometimes been reported to predict tinnitus-related distress [78].

Epidemiological studies show that tinnitus becomes more common with age, probably due to more frequent or severe hearing loss [11]. Studies have shown that most people with tinnitus show high-frequency hearing loss which is often correlated with highfrequency tinnitus perception [11, 79]. However, hearing loss and tinnitus-related distress are usually uncorrelated – highlighting the crucial importance of psychological third variables. For example, hearing loss can be measured in approximately 90% of people with tinnitus; however, most people with hearing loss report not have tinnitus, irrespective of the severity of the hearing loss [41]. It is possible that interactions of older age and hearing loss, cognitive changes, and anxiety or depression may contribute to distressing tinnitus experiences at older ages [80].

4.4 Cognitive influences

The role of cognitive factors in hearing loss, tinnitus or tinnitus-related distress is currently investigated intensively [81-83]. The term "cognition" denotes the sum of all thought and perception processes which can be conscious or unconscious [84], and many of which decline with age [85]. Clinically, it is noticeable that patients with chronic tinnitus often report difficulties that at least partially suggest cognitive influences - such as concentration or working memory difficulties [56]. However, in context of strong construct overlaps, it must be critically examined whether these difficulties might actually reflect depression-related difficulties that are merely attributed to the tinnitus symptom. Cognitive processes are closely interlinked with affective influences such as anxiety and depression [86, 87], as well as audiological processes [88]. Thus, whilst cognitive processes are relevant to hearing [89], hearing loss may conversely contribute to cognitive difficulties [82, 90, 91] as well as depressive experiences [92].

On a theoretical level, tinnitus may reduce individuals' cognitive capacity and executive control which are needed to perform tasks. Cognitive functions such as attention, concentration, and executive control are prefrontally controlled, and dysfunction of frontal neural processes may thus impede habituation to the tinnitus sound and, in interaction with the limbic system, reflect subjective distress experiences [93, 94]. For example, individuals with chronic tinnitus showed difficulties in attention and memory tests [95–97]. Recent neuropsychological studies [81,98] further suggest that individuals with chronic tinnitus may exhibit executive difficulties, involving e.g. "stimulus inhibition" (i.e., the ability to suppress automatic responses) or "set-shifting" abilities (i.e., the ability to switch between different stimulus sources). These processes may, in turn, be linked to individuals' hearing ability and listening effort [99]. The "cognitive-perceptual load theory" [100] postulates that continuous perception of the tinnitus sound uses perceptual resources - which are consequently no longer available for other sensory environmental stimuli. Moreover, the tinnitus sound may use central resources such as stimulus discrimination and working memory capacities thus facilitating an increased cognitive load.

Depression research has linked interactions of reduced executive control and its effects on limbic circuits to patients' experiences of emotional excitability and reduced emotion regulation ability [101]. Negative effects of depression on cognitive processes such as working memory are also well established [102]. For chronic tinnitus patients, Neff et al. [83] observed an association between tinnitus-related distress and decreased crystalline intelligence and stimulus processing speed.

Overall, these results once again emphasize that, in addition to careful clarification of otological, audiological and internistic influences, psychological factors – including cognitive factors – ought to be taken into account for assessment and treatment planning.

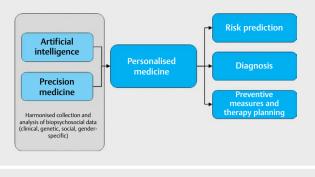


Fig. 3 Outlook – personalised medicine.

5. Treatment options

Current guidelines recommend the provision of hearing aids for people with hearing loss and chronic tinnitus alongside psychoeducational "counselling" and psychotherapeutic approaches [103]. Hearing aids may positively influence tinnitus-related distress [104, 105]. For example, a recent randomized cross-over study demonstrated that a specific hearing aid fitting could reduce tinnitusrelated distress in individuals with chronic tinnitus and mild-to-moderate hearing loss [106]. Whether hearing aids can also have a positive effect on cognitive difficulties is controversially discussed [80, 107–110]. Psychotherapeutic approaches are is the treatment option of choice for individuals who experience the tinnitus sound as highly distressing [104]. A recent review concluded that cognitive behavioral therapies significantly increased the quality of life of patients with chronic tinnitus [111]. Whilst psychodynamic therapy approaches have not been studied in randomized-controlled trials, effectiveness can still be assumed, as psychodynamically oriented multimodal treatment approaches achieve good results [112, 113]. Regarding mediators of treatment change, Cima et al. [114] reported that reductions in tinnitus-related anxiety significantly predicted treatment success of a special treatment developed by the authors. Another study that investigated mediators of treatment change for a multimodal treatment program identified the psychotherapeutic amelioration of "worry," "depressiveness," and "emotional tension" as mediators of treatment success [29].

6. Conclusion and outlook

The assessment, formulation and treatment of chronic tinnitus ought to be based on otological, audiological, psychosomatic and psychological diagnostics. The latter should apply validated questionnaires which do not apply mere symptom checklists, but which assess dimensions of psychological experiences and stimulus processing (e.g., catastrophizing tendencies, optimism-pessimism, or self-efficacy [115, 116]). Age- or mood-associated cognitive abnormalities should be assessed neuro-psychologically, where indicated. Treatment procedures should be derived based on an individual psychosomatic case conceptualization, that links medical, audiological, and psychological aspects of the tinnitus sound within a broader, holistic context [19].

German and European guidelines also recommend a combination of multimodal therapy components that are tailored to individuals' needs [104]. For individuals with hearing loss, hearing aids are the initial treatment option of choice, where applicable. Preliminary evidence suggests that the use of hearing aids can benefit tinnitus-related distress for patients with mild-to-moderate hearing loss [106]. In cases of profound hearing loss, a cochlear implant should be considered [117–119].

The current gold standard for treating tinnitus-related distress are psychotherapeutic approaches that favorably influence tinnitus-related distress, quality of life as well as anxiety and depressivity [111]. Such treatment approaches must be individually formulated [21, 29] and consider sociocultural [120] as well as gender-[121, 122] or age-associated influences [123]. In case of severe emotional distress, day-care or inpatient treatments may be indicated.

In future, the field can expect further improvements in assessment and therapy. Novel research frameworks focus on dimensional (not categorical) conceptualizations of psychological distress [124–126], biomarkers of tinnitus-related distress [33, 35, 127] as well as refined psychotherapeutic treatment frameworks [128]. In addition, the importance of unified data collections [129–131] or methodological advances in big data analysis are of increasing importance [31, 58]. These developments pave the way for personalized medicine approaches across chronic conditions and multidimensional stress experiences (**> Fig. 3**).

Conflict of Interest

The authors declare that they have no conflict of interest.

References

- De Ridder D, Schlee W, Vanneste S et al. Tinnitus and tinnitus disorder: Theoretical and operational definitions (an international multidisciplinary proposal). Prog Brain Res 2021; 260: 1–25
- [2] Trevis KJ, McLachlan NM, Wilson SJ. Psychological mediators of chronic tinnitus: the critical role of depression. J Affect Disord 2016; 204: 234–240
- [3] Wallhäusser-Franke E, D'Amelio R, Glauner A et al. Transition from acute to chronic Tinnitus: Predictors for the Development of chronic Distressing Tinnitus. Front Neurol 2017; 8: 605
- [4] Zirke N, Seydel C, Arsoy D et al. Analysis of mental disorders in tinnitus patients performed with Composite International Diagnostic Interview. Qual Life Res 2013; 22: 2095–2104
- [5] Biswas R, Lugo A, Akeroyd MA et al. Tinnitus prevalence in Europe: a multi-country cross-sectional population study. Lancet Reg Health-Eur 2022; 12: 100250
- [6] Trochidis I, Lugo A, Borroni E et al. Systematic review on healthcare and societal costs of tinnitus. Int J Environ Res Public Health 2021; 18: 6881
- [7] Tziridis K, Friedrich J, Brüeggemann P et al. Estimation of Tinnitus-Related Socioeconomic Costs in Germany. Int J Environ Res Public Health 2022; 19: 10455
- [8] Park B, Choi HG, Lee H-J et al. Analysis of the prevalence of and risk factors for tinnitus in a young population. Otol Neurotol 2014; 35: 1218–1222

- [9] Kim H-J, Lee H-J, An S-Y et al. Analysis of the prevalence and associated risk factors of tinnitus in adults. PLoS One 2015; 10: e0127578
- [10] König O, Schaette R, Kempter R et al. Course of hearing loss and occurrence of tinnitus. Hear Res 2006; 221: 59–64
- [11] Savastano M. Tinnitus with or without hearing loss: are its characteristics different? Eur Arch Otorhinolaryngol 2008; 265: 1295–1300
- [12] Baguley D, McFerran D, Hall D. Tinnitus. The Lancet 2013; 382: 1600–1607
- [13] Deklerck AN, Debacker JM, Keppler H et al. Identifying non-otologic risk factors for tinnitus: a systematic review. Clin Otolaryngol 2020; 45: 775–787
- [14] Gomaa MAM, Elmagd MHA, Elbadry MM et al. Depression, Anxiety and Stress Scale in patients with tinnitus and hearing loss. Eur Arch Otorhinolaryngol 2014; 271: 2177–2184
- [15] Zenner HP, Delb W, Kröner-Herwig B et al. On the interdisciplinary S3 guidelines for the treatment of chronic idiopathic tinnitus. Hno 2015; 63: 419–427
- [16] Schmitt C, Patak M, Kroner-Herwig B. Stress and the onset of sudden hearing loss and tinnitus. Int Tinnitus J 2000; 6: 41–49
- [17] Georgiewa P, Klapp BF, Fischer F et al. An integrative model of developing tinnitus based on recent neurobiological findings. Med Hypotheses 2006; 66: 592–600
- [18] Andersson G. Psychological aspects of tinnitus and the application of cognitive – behavioral therapy. Clin Psychol Rev 2002; 22: 977–990
- [19] Boecking B, Brueggemann P, Mazurek B. Tinnitus: psychosomatische Aspekte. HNO 2019; 1–16
- [20] Heinecke K, Weise C, Schwarz K et al. Physiological and psychological stress reactivity in chronic tinnitus. J Behav Med 2008; 31: 179–188
- [21] Biehl R, Boecking B, Brueggemann P et al. Personality Traits, Perceived Stress, and Tinnitus-Related Distress in Patients With Chronic Tinnitus: Support for a Vulnerability-Stress Model. Front Psychol 2020; 10:
- [22] McKenna L, Handscomb L, Hoare DJ et al. A scientific cognitive-behavioral model of tinnitus: novel conceptualizations of tinnitus distress. Front Neurol 2014; 5: 196
- [23] Ivansic D, Dobel C, Volk GF et al. Results of an Interdisciplinary Day Care Approach for Chronic Tinnitus Treatment: A Prospective Study Introducing the Jena Interdisciplinary Treatment for Tinnitus. Front Aging Neurosci 2017; 9: 192
- [24] Seydel C, Haupt H, Szczepek AJ et al. Three years later: report on the state of well-being of patients with chronic tinnitus who underwent modified tinnitus retraining therapy. Audiol Neurotol 2015; 20: 26–38
- [25] Brueggemann P, Mebus W, Boecking B et al. Dimensions of Tinnitus-Related Distress. Brain Sci 2022; 12: 275
- [26] Mirowsky J, Ross CE. Age and depression. J Health Soc Behav 1992; 187–205
- [27] Kleinstäuber M, Weise C. Psychosocial variables that predict chronic and disabling tinnitus: a systematic review. Behav Neurosci Tinnitus 2020; 361–380
- [28] Olderog M, Langenbach M, Michel O et al. Prädiktoren und Mechanismen der ausbleibenden Tinnitus-Toleranzentwicklung-eine Längsschnittstudie. Laryngo-Rhino-Otol 2004; 83: 5–13
- [29] Boecking B, Rose M, Brueggemann P et al. Two birds with one ssound.-Addressing depressive symptoms, emotional tension and worry improves tinnitus-related distress and affective pain perceptions in patients with chronic tinnitus. Plos One 2021; 16: e0246747
- [30] Cederroth CR, Gallus S, Hall DA et al. Towards an understanding of tinnitus heterogeneity. Front Aging Neurosci 2019; 53:
- [31] Niemann U, Brueggemann P, Boecking B et al. Phenotyping chronic tinnitus patients using self-report questionnaire data: Cluster analysis and visual comparison. Sci Rep 2020; 10: 1–10

- [32] Hiller W, Janca A, Burke KC. Association between tinnitus and somatoform disorders. J Psychosom Res 1997; 43: 613–624
- [33] Basso L, Boecking B, Neff P et al. Hair-cortisol and hair-BDNF as biomarkers of tinnitus loudness and distress in chronic tinnitus. Sci Rep 2022; 12: 1–14
- [34] Besteher B, Gaser C, Ivanšić D et al. Chronic tinnitus and the limbic system: reappraising brain structural effects of distress and affective symptoms. NeuroImage Clin 2019; 24: 101976
- [35] Boecking B, Klasing S, Walter M et al. Vascular Metabolic Risk Factors and Psychological Stress in Patients with Chronic Tinnitus. Nutrients 2022; 14: 2256
- [36] Cederroth CR, Kähler AK, Sullivan PF et al. Genetics of tinnitus: time to biobank phantom sounds. Front Genet 2017; 8: 110
- [37] Haider HF, Hoare DJ, Ribeiro SF et al. Evidence for biological markers of tinnitus: A systematic review. Prog Brain Res 2021; 262: 345–398
- [38] Paraskevopoulos E, Dobel C, Wollbrink A et al. Maladaptive alterations of resting state cortical network in Tinnitus: A directed functional connectivity analysis of a larger MEG data set. Sci Rep 2019; 9: 1–11
- [39] Simonetti P, Oiticica J. Tinnitus neural mechanisms and structural changes in the brain: The contribution of neuroimaging research. Int Arch Otorhinolaryngol 2015; 19: 259–265
- [40] Auerbach BD, Rodrigues PV, Salvi RJ. Central gain control in tinnitus and hyperacusis. Front Neurol 2014; 5: 206
- [41] Sedley W. Tinnitus: does gain explain? Neuroscience 2019; 407: 213–228
- [42] De Ridder D, Elgoyhen AB, Romo R et al. Phantom percepts: tinnitus and pain as persisting aversive memory networks. Proc Natl Acad Sci 2011; 108: 8075–8080
- [43] Elgoyhen AB, Langguth B, De Ridder D et al. Tinnitus: perspectives from human neuroimaging. Nat Rev Neurosci 2015; 16: 632
- [44] Eggermont JJ. Correlated neural activity as the driving force for functional changes in auditory cortex. Hear Res 2007; 229: 69–80
- [45] Georgiewa P, Szczepek AJ, Rose M et al. Cerebral processing of emotionally loaded acoustic signals by tinnitus patients. Audiol Neurotol 2016; 21: 80–87
- [46] Bhatt JM, Bhattacharyya N, Lin HW. Relationships between tinnitus and the prevalence of anxiety and depression. The Laryngoscope 2017; 127: 466–469
- [47] Ivansic D, Besteher B, Gantner J et al. Psychometric assessment of mental health in tinnitus patients, depressive and healthy controls. Psychiatry Res 2019; 281: 112582
- [48] Konzag TA, Rübler D, Bandemer-Greulich U et al. Psychological comorbidity in subacute and chronic tinnitus outpatients. Z Psychosom Med Psychother 2005; 51: 247–260
- [49] McCormack A, Edmondson-Jones M, Fortnum H et al. Investigating the association between tinnitus severity and symptoms of depression and anxiety, while controlling for neuroticism, in a large middle-aged UK population. Int J Audiol 2015; 54: 599–604
- [50] Pattyn T, Van Den Eede F, Vanneste S et al. Tinnitus and anxiety disorders: a review. Hear Res 2016; 333: 255–265
- [51] Pinto PCL, Marcelos CM, Mezzasalma MA et al. Tinnitus and its association with psychiatric disorders: systematic review. J Laryngol Otol 2014; 128: 660–664
- [52] Salazar JW, Meisel K, Smith ER et al. Depression in patients with tinnitus: a systematic review. Otolaryngol Neck Surg 2019; 161: 28–35
- [53] Ziai K, Moshtaghi O, Mahboubi H et al. Tinnitus patients suffering from anxiety and depression: a review. Int Tinnitus J 2017; 21: 68–73
- [54] Sahin C, Aras HI, Yilmaz MS. Somatoform disorders in patients with chronic subjective tinnitus. Eur Arch Otorhinolaryngol 2016; 273: 3603–3607

- [55] Asnis GM, Majeed K, Henderson MA et al. An examination of the relationship between insomnia and tinnitus: A review and recommendations. Clin Med Insights. Psychiatry 2018; 9: 1179557318781078
- [56] Mohamad N, Hoare DJ, Hall DA. The consequences of tinnitus and tinnitus severity on cognition: a review of the behavioural evidence. Hear Res 2016; 332: 199–209
- [57] Goebel G, Decot E, Marek A. Entscheidungshilfen bei Diagnostik und Wahl psychologischer Behandlungsmethoden. HNO 2001; 49: 1036–1046
- [58] Niemann U, Brueggemann P, Boecking B et al. Development and internal validation of a depression severity prediction model for tinnitus patients based on questionnaire responses and socio-demographics. Sci Rep 2020; 10: 1–9
- [59] Langguth B, Kleinjung T, Landgrebe M. Severe tinnitus and depressive symptoms: a complex interaction. Otolaryngol Neck Surg 2011; 145: 519–519
- [60] Betz LT, Mühlberger A, Langguth B et al. Stress reactivity in chronic tinnitus. Sci Rep 2017; 7: 41521
- [61] Budd RJ, Pugh R. The relationship between locus of control, tinnitus severity, and emotional distress in a group of tinnitus sufferers. J Psychosom Res 1995; 39: 1015–1018
- [62] Mazurek B, Szczepek AJ, Hebert S. Stress and Tinnitus. HNO 2015; 63: 258–265
- [63] Mazurek B, Boecking B, Brueggemann P. Association between stress and tinnitus – new aspects. Otol Neurotol 2019; 40: e467–e473
- [64] Møller AR. Similarities between tinnitus and pain. In: Textbook of tinnitus. Springer; 2011: 113–120
- [65] Gatchel RJ, Peng YB, Peters ML et al. The biopsychosocial approach to chronic pain: scientific advances and future directions. Psychol Bull 2007; 133: 581
- [66] Kerns RD, Sellinger J, Goodin BR. Psychological treatment of chronic pain. Annu Rev Clin Psychol 2011; 7: 411–434
- [67] Folmer RL, Griest SE, Martin WH. Chronic tinnitus as phantom auditory pain. Otolaryngol Neck Surg 2001; 124: 394–400
- [68] Rauschecker JP, May ES, Maudoux A et al. Frontostriatal gating of tinnitus and chronic pain. Trends Cogn Sci 2015; 19: 567–578
- [69] Boecking B, von Sass J, Sieveking A et al. Tinnitus-related distress and pain perceptions in patients with chronic tinnitus – Do psychological factors constitute a link? PloS One 2020; 15: e0234807
- [70] De Ridder D, Vanneste S, Weisz N et al. An integrative model of auditory phantom perception: tinnitus as a unified percept of interacting separable subnetworks. Neurosci Biobehav Rev 2014; 44: 16–32
- [71] Seydell-Greenwald A, Leaver AM, Turesky TK et al. Functional MRI evidence for a role of ventral prefrontal cortex in tinnitus. Brain Res 2012; 1485: 22–39
- [72] Henry JA, Meikle MB. Psychoacoustic measures of tinnitus. J Am Acad Audiol 2000; 11: 138–155
- [73] Herrmann B, Butler BE. Hearing loss and brain plasticity: the hyperactivity phenomenon. Brain Struct Funct 2021; 226: 2019– 2039
- [74] Roberts LE, Eggermont JJ, Caspary DM et al. Ringing ears: the neuroscience of tinnitus. J Neurosci 2010; 30: 14972–14979
- [75] Shore SE, Wu C. Mechanisms of noise-induced tinnitus: insights from cellular studies. Neuron 2019; 103: 8–20
- [76] Langguth B, Kreuzer PM, Kleinjung T et al. Tinnitus: causes and clinical management. Lancet Neurol 2013; 12: 920–930
- [77] Shargorodsky J, Curhan GC, Farwell WR. Prevalence and characteristics of tinnitus among US adults. Am J Med 2010; 123: 711–718

- [78] Langguth B, Landgrebe M, Schlee W et al. Different patterns of hearing loss among tinnitus patients: a latent class analysis of a large sample. Front Neurol 2017; 8: 46
- [79] Satar B, Kapkin O, Özkaptan Y. Evaluation of cochlear function in patients with normal hearing and tinnitus: a distortion product otoacoustic emission study. Turk J Ear Nose Throat 2003; 10: 177–182
- [80] Jafari Z, Kolb BE, Mohajerani MH. Age-related hearing loss and tinnitus, dementia risk, and auditory amplification outcomes. Ageing Res Rev 2019; 56: 100963
- [81] Clarke NA, Henshaw H, Akeroyd MA et al. Associations between subjective tinnitus and cognitive performance: systematic review and meta-analyses. Trends Hear 2020; 24: 2331216520918416
- [82] Loughrey DG, Kelly ME, Kelley GA et al. Association of age-related hearing loss with cognitive function, cognitive impairment, and dementia: a systematic review and meta-analysis. JAMA Otolaryngol Neck Surg 2018; 144: 115–126
- [83] Neff P, Simões J, Psatha S et al. The impact of tinnitus distress on cognition. Sci Rep 2021; 11: 1–9
- [84] Kihlstrom JF. Conscious versus unconscious cognition. Nat Cogn 1999; 173–203
- [85] Park DC, Reuter-Lorenz P. The adaptive brain: aging and neurocognitive scaffolding. Annu Rev Psychol 2009; 60: 173
- [86] Gotlib IH, Joormann J. Cognition and depression: current status and future directions. Annu Rev Clin Psychol 2010; 6: 285
- [87] Maloney EA, Sattizahn JR, Beilock SL. Anxiety and cognition. Wiley Interdiscip Rev Cogn Sci 2014; 5: 403–411
- [88] Arlinger S, Lunner T, Lyxell B et al. The emergence of cognitive hearing science. Scand J Psychol 2009; 50: 371–384
- [89] Fulton SE, Lister JJ, Bush ALH et al. Mechanisms of the hearing –cognition relationship. In: Seminars in hearing. Thieme Medical Publishers; 2015: 140–149
- [90] Lin FR, Thorpe R, Gordon-Salant S et al. Hearing loss prevalence and risk factors among older adults in the United States. J Gerontol Ser Biomed Sci Med Sci 2011; 66: 582–590
- [91] Lin FR, Yaffe K, Xia J et al. Hearing loss and cognitive decline in older adults. JAMA Intern Med 2013; 173: 293–299
- [92] Deal JA, Reed NS, Kravetz AD et al. Incident hearing loss and comorbidity: a longitudinal administrative claims study. JAMA Otolaryngol Neck Surg 2019; 145: 36–43
- [93] Rauschecker JP, Leaver AM, Mühlau M. Tuning out the noise: limbic-auditory interactions in tinnitus. Neuron 2010; 66: 819–826
- [94] Roberts LE, Husain FT, Eggermont JJ. Role of attention in the generation and modulation of tinnitus. Neurosci Biobehav Rev 2013; 37: 1754–1773
- [95] Nagaraj MK, Bhaskar A, Prabhu P. Assessment of auditory working memory in normal hearing adults with tinnitus. Eur Arch Otorhinolaryngol 2020; 277: 47–54
- [96] Rossiter S, Stevens C, Walker G. Tinnitus and its effect on working memory and attention 2006
- [97] Waechter S, Wilson WJ, Brännström JK. The impact of tinnitus on working memory capacity. Int J Audiol 2021; 60: 274–281
- [98] Jagoda L, Giroud N, Neff P et al. Speech perception in tinnitus is related to individual distress level-A neurophysiological study. Hear Res 2018; 367: 48–58
- [99] Degeest S, Kestens K, Keppler H. Investigation of the Relation Between Tinnitus, Cognition, and the Amount of Listening Effort. J Speech Lang Hear Res 2022; 65: 1988–2002
- [100] Khan RA, Husain FT. Tinnitus and cognition: Can load theory help us refine our understanding? Laryngoscope Investig Otolaryngol 2020; 5: 1197–1204

- [101] Pitsillou E, Bresnehan SM, Kagarakis EA et al. The cellular and molecular basis of major depressive disorder: towards a unified model for understanding clinical depression. Mol Biol Rep 2020; 47: 753–770
- [102] Christopher G, MacDonald J. The impact of clinical depression on working memory. Cognit Neuropsychiatry 2005; 10: 379–399
- [103] Mazurek B, Hesse G, Dobel C et al. Chronic Tinnitus: Diagnosis and Treatment. Dtsch Ärztebl Int 2022; 119: 219
- [104] Cima RFF, Mazurek B, Haider H et al. A multidisciplinary European guideline for tinnitus: diagnostics, assessment, and treatment. Hno 2019; 67: 10–42
- [105] Hoare DJ, Edmondson-Jones M, Sereda M et al. Amplification with hearing aids for patients with tinnitus and co-existing hearing loss. Cochrane Database Syst Rev 2014
- [106] Boecking B, Rausch L, Psatha S et al. Hearing Therapy Improves Tinnitus-Related Distress in Mildly Distressed Patients with Chronic Tinnitus and Mild-to-Moderate Hearing Loss: A Randomized-Controlled Cross-Over Design. J Clin Med 2022; 11: 1764
- [107] Dawes P, Emsley R, Cruickshanks KJ et al. Hearing loss and cognition: the role of hearing aids, social isolation and depression. PloS One 2015; 10: e0119616
- [108] Sanders ME, Kant E, Smit AL et al. The effect of hearing aids on cognitive function: A systematic review. PloS One 2021; 16: e0261207
- [109] Sarant J, Harris D, Busby P et al. The effect of hearing aid use on cognition in older adults: can we delay decline or even improve cognitive function? J Clin Med 2020; 9: 254
- [110] van Hooren SA, Anteunis LJ, Valentijn SA et al. Does cognitive function in older adults with hearing impairment improve by hearing aid use? Int J Audiol 2005; 44: 265–271
- [111] Fuller T, Cima R, Langguth B et al. Cognitive behavioural therapy for tinnitus. Cochrane Database Syst Rev 2020
- [112] Hesse G, Mazurek B. Chronic tinnitus-Therapeutic aspects, based on the new german guideline. Dtsch Med Wochenschr 1946; 2022: 682–687
- [113] Schaaf H, Weis S, Hesse G. Catamnesis results of an inpatient neuro-otologic and psychosomatic tinnitus therapy 1–5 years after discharge. Eur Arch Otorhinolaryngol 2017; 274: 701–710
- [114] Cima RF, van Breukelen G, Vlaeyen JW. Tinnitus-related fear: mediating the effects of a cognitive behavioural specialised tinnitus treatment. Hear Res 2018; 358: 86–97
- [115] Cima RF, Crombez G, Vlaeyen JW. Catastrophizing and fear of tinnitus predict quality of life in patients with chronic tinnitus. Ear Hear 2011; 32: 634–641
- [116] Kratzsch V, Goebel G. Current aspects of tinnitus and depression. HNO 2018; 66: 188–197
- [117] Brueggemann P, Szczepek AJ, Klee K et al. In patients undergoing cochlear implantation, psychological burden affects tinnitus and the overall outcome of auditory rehabilitation. Front Hum Neurosci 2017; 11: 226
- [118] Knopke S, Szczepek AJ, Häussler SM et al. Cochlear implantation of bilaterally deafened patients with tinnitus induces sustained decrease of tinnitus-related distress. Front Neurol 2017; 8: 158
- [119] Olze H, Szczepek AJ, Haupt H et al. Cochlear implantation has a positive influence on quality of life, tinnitus, and psychological comorbidity. The Laryngoscope 2011; 121: 2220–2227
- [120] McCormack A, Edmondson-Jones M, Somerset S et al. A systematic review of the reporting of tinnitus prevalence and severity. Hear Res 2016; 337: 70–79
- [121] Basso L, Boecking B, Brueggemann P et al. Gender-Specific Risk Factors and Comorbidities of Bothersome Tinnitus. Front Neurosci 2020; 14: 706: 1–15

- [122] Niemann U, Boecking B, Brueggemann P et al. Gender-Specific Differences in Patients with Chronic Tinnitus – Baseline Characteristics and Treatment Effects. Front Neurosci 2020; 14: 487
- [123] Hoare DJ, Hall DA. Clinical guidelines and practice: a commentary on the complexity of tinnitus management. Eval Health Prof 2011; 34: 413–420
- [124] Cuthbert BN. The RDoC framework: facilitating transition from ICD/ DSM to dimensional approaches that integrate neuroscience and psychopathology. World Psychiatry 2014; 13: 28–35
- [125] Cuthbert BN, Insel TR. Toward the future of psychiatric diagnosis: the seven pillars of RDoC. BMC Med 2013; 11: 1–8
- [126] Kotov R, Krueger RF, Watson D et al. The Hierarchical Taxonomy of Psychopathology (HiTOP): A dimensional alternative to traditional nosologies. J Abnorm Psychol 2017; 126: 454
- [127] Basso L, Boecking B, Neff P et al. Psychological Treatment Effects Unrelated to Hair-Cortisol and Hair-BDNF Levels in Chronic Tinnitus. Front Psychiatry 2022; 13: 1–20

- [128] Dimidjian S, Arch JJ, Schneider RL et al. Considering meta-analysis, meaning, and metaphor: A systematic review and critical examination of "third wave" cognitive and behavioral therapies. Behav Ther 2016; 47: 886–905
- [129] Hall DA, Haider H, Kikidis D et al. Toward a global consensus on outcome measures for clinical trials in tinnitus: report from the First International Meeting of the COMiT Initiative, November 14, 2014, Amsterdam, The Netherlands. Trends Hear 2015; 19: 2331216515580272
- [130] Henry JA, Roberts LE, Caspary DM et al. Underlying mechanisms of tinnitus: review and clinical implications. J Am Acad Audiol 2014; 25: 005–022
- [131] Schlee W, Schoisswohl S, Staudinger S et al. Towards a unification of treatments and interventions for tinnitus patients: The EU research and innovation action UNITI. Prog Brain Res 2021; 260: 441–451