university of groningen

University Medical Center Groningen

University of Groningen

The stochastic resonance model of auditory perception

Schilling, Achim; Tziridis, Konstantin; Schulze, Holger; Krauss, Patrick

Published in:
Tinnitus - An Interdisciplinary Approach Towards Individualized Treatment

DOI:
10.1016/bs.pbr.2021.01.025

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2021

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Schilling, A., Tziridis, K., Schulze, H., & Krauss, P. (2021). The stochastic resonance model of auditory perception: A unified explanation of tinnitus development, Zwicker tone illusion, and residual inhibition. In B. Langguth, T. Kleinjung, D. De Ridder, W. Schlee, S. Vanneste, & S. Vanneste (Eds.), *Tinnitus - An Interdisciplinary Approach Towards Individualized Treatment: Towards understanding the complexity of tinnitus* (pp. 139-157). (Progress in Brain Research; Vol. 262). Elsevier Bedrijfsinformatie b.v.. https://doi.org/10.1016/bs.pbr.2021.01.025

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the “Taverne” license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment.

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Download date: 05-06-2022

CHAPTER

6

The stochastic resonance model of auditory perception: A unified explanation of tinnitus development, Zwicker tone illusion, and residual inhibition

Achim Schilling[a,b], Konstantin Tziridis[a], Holger Schulze[a], and Patrick Krauss[a,b,c,d,*]

[a]*Neuroscience Lab, Experimental Otolaryngology, University Hospital Erlangen, Erlangen, Germany*

[b]*Cognitive Computational Neuroscience Group at the Chair of English Philology and Linguistics, Friedrich-Alexander University Erlangen-Nürnberg (FAU), Erlangen, Germany*

[c]*FAU Linguistics Lab, Friedrich-Alexander University Erlangen-Nürnberg (FAU), Erlangen, Germany*

[d]*Department of Otorhinolaryngology/Head and Neck Surgery, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands*

**Corresponding author: Tel: +4991318533911, e-mail address: patrick.krauss@uk-erlangen.de*

Abstract

Stochastic resonance (SR) has been proposed to play a major role in auditory perception, and to maintain optimal information transmission from the cochlea to the auditory system. By this, the auditory system could adapt to changes of the auditory input at second or even sub-second timescales. In case of reduced auditory input, somatosensory projections to the dorsal cochlear nucleus would be disinhibited in order to improve hearing thresholds by means of SR. As a side effect, the increased somatosensory input corresponding to the observed tinnitus-associated neuronal hyperactivity is then perceived as tinnitus. In addition, the model can also explain transient phantom tone perceptions occurring after ear plugging, or the Zwicker tone illusion. Vice versa, the model predicts that via stimulation with acoustic noise, SR would not be needed to optimize information transmission, and hence somatosensory noise would be tuned down, resulting in a transient vanishing of tinnitus, an effect referred to as residual inhibition.

Progress in Brain Research, Volume 262, ISSN 0079-6123, https://doi.org/10.1016/bs.pbr.2021.01.025
Copyright © 2021 Elsevier B.V. All rights reserved.

Keywords

Auditory phantom perception, Somatosensory projections, Dorsal cochlear nucleus, Speech perception, Tinnitus, Zwicker tone, Residual inhibition, Stochastic resonance

1 Stochastic resonance

In engineering, the term *noise*, defined as undesirable disturbances or fluctuations, is considered to be the "fundamental enemy" (McDonnell and Abbott, 2009) for error-free information transmission, processing, and communication. However, a vast and even increasing number of studies show the various benefits of noise in the context of signal detection and processing. Here, the most important phenomena are called stochastic resonance (McDonnell and Abbott, 2009), coherence resonance (Pikovsky and Kurths, 1997), and recurrence resonance (Krauss et al., 2019a).

The term stochastic resonance (SR), which has been introduced by Benzi in 1981 (Benzi et al., 1981), refers to the phenomenon that signals otherwise sub-threshold for a given sensor can be detected by adding a random signal, i.e. noise, of appropriate intensity to the sensor input (Gammaitoni et al., 1998; Moss et al., 2004). Fig. 1 illustrates this principle.

SR has been found ubiquitously in nature in a broad range of systems from physical to biological contexts (Hänggi, 2002; Wiesenfeld and Moss, 1995). In particular in neuroscience, SR has been demonstrated to play an essential role in virtually all kinds of systems (Faisal et al., 2008): from tactile (Collins et al., 1996; Douglass et al., 1993), auditory (Mino, 2014) and visual (Aihara et al., 2008) perception (Ward et al., 2002), through memory retrieval (Usher and Feingold, 2000) and cognition (Chandrasekharan et al., 2005), to behavioral control (Kitajo et al., 2003; Ward et al., 2002). SR explains how the brain processes information in noisy environments at each level of scale from single synapses (Stacey and Durand, 2001), through individual neurons (Kosko and Mitaim, 2003; Nozaki et al., 1999), to complete networks (Gluckman et al., 1996).

In self-adaptive signal detection systems exploiting SR, the optimum intensity of the noise is continuously adjusted so that information transmission is maximized, even if the characteristics and statistics of the input signal change (Fig. 2). For this processing principle, the term adaptive SR has been coined (Krauss et al., 2017; Mitaim and Kosko, 1998, 2004; Wenning and Obermayer, 2003).

2 Tinnitus development

In a number of recently published studies, we demonstrated theoretically and empirically that SR might be a major processing principle of the auditory system that serves to partially compensate for acute or chronic hearing loss (Krauss et al., 2016, 2017, 2018, 2019b; Gollnast et al., 2017). According to our model, the noise required for SR is generated within the brain and then perceived as a phantom sound. We have

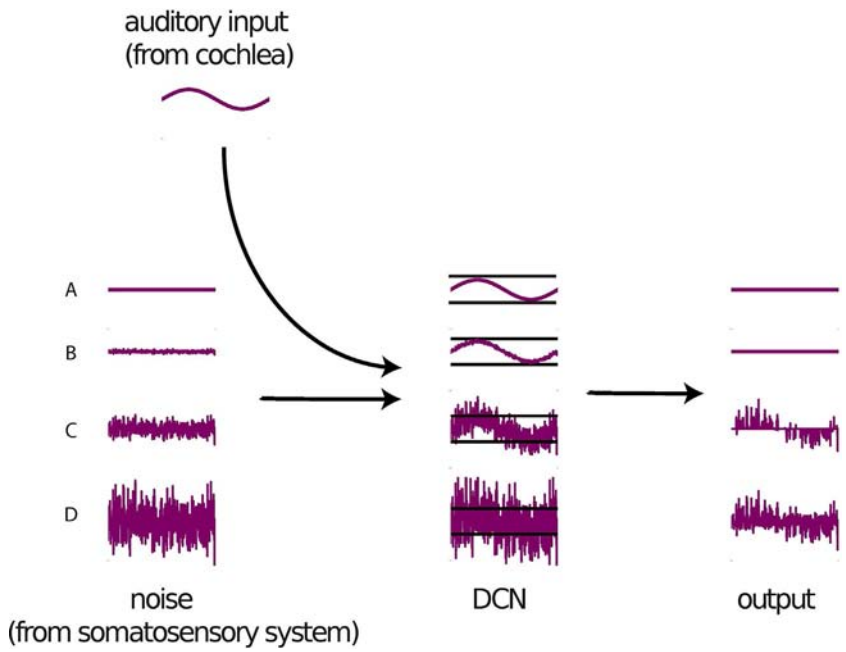

FIG. 1

Principle of stochastic resonance. The auditory input without any added noise is too weak to pass the threshold (A). Also if the intensity of added noise is too weak, the sum of auditory input and noise cannot pass the threshold (B). Both cases result in zero output. In contrast, if the optimal amount of noise is added to the signal before thresholding, the resulting output's envelope resembles the auditory input signal (C). However, if the noise intensity is further increased, the signal vanishes again in the noisy output (D).

proposed that it corresponds to increased spontaneous neuronal firing rates in early processing stages of the auditory brain stem - a phenomenon which is frequently observed in both humans with subjective tinnitus (Ahlf et al., 2012; Tziridis et al., 2015; Wang et al., 1997; Wu et al., 2016) and animal models, where the presence of tinnitus is tested using behavioral paradigms (Gerum et al., 2019, Schilling et al., 2017, Turner et al., 2006). Furthermore, tinnitus is assumed to be virtually always caused by some kind of either apparent (Heller 2003; König et al., 2006; Nelson & Chen 2004; Shore et al., 2016) or hidden hearing loss (Liberman & Liberman 2015; Schaette & McAlpine 2011). From this point of view, auditory phantom perceptions like tinnitus (or even the Zwicker tone, cf. below) seem to be a side effect of an adaptive mechanism within the auditory system whose primary purpose is to compensate for reduced input through continuous optimization of information transmission (Krauss et al., 2016, 2017, 2018, 2019b). This new interpretation may also explain why auditory sensitivity is increased in tinnitus ears (Gollnast et al., 2017; Hébert et al., 2013): the increased amount of neural noise during tinnitus improves auditory sensitivity by means of SR.

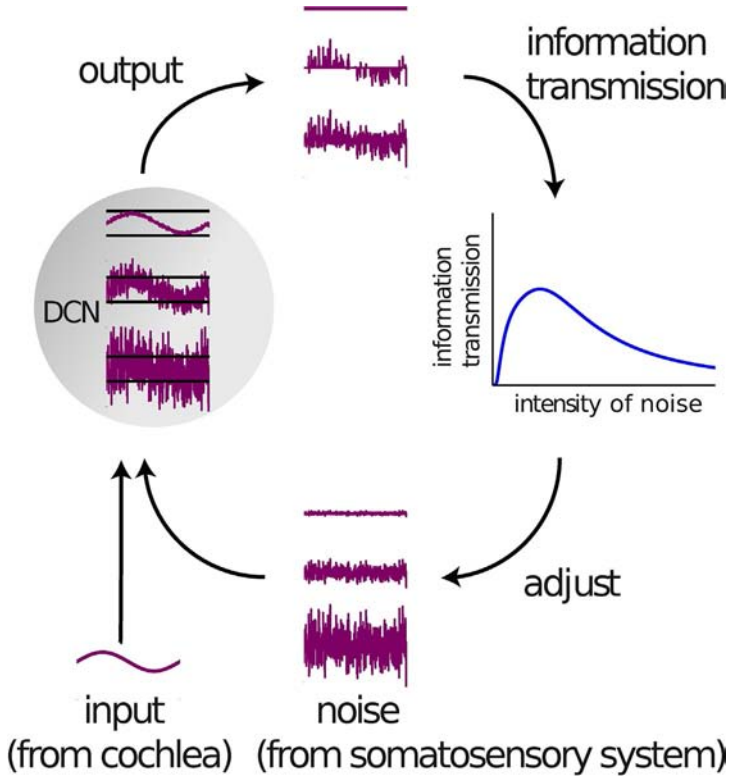

FIG. 2

Adaptive stochastic resonance control circuit in the DCN. In self-adaptive signal detection systems based on SR, the optimum noise level is continuously adjusted via a feedback loop, so that the system's response in terms of information throughput remains optimal, even if the properties of the input signal change. In the SR model of tinnitus development, this process takes place in the DCN. The input signal comes from the cochlea, the noise from the somatosensory system.

According to our model, the noise intensity is adjusted independently in each frequency channel. This is in line with several findings. The dorsal cochlear nucleus (DCN) has been shown to be the earliest processing stage where acoustic trauma, including complete cochlea ablation (Zacharek et al., 2002), causes increased spontaneous firing rates (Kaltenbach & Afman 2000; Kaltenbach et al., 1998; Wu et al., 2016; Zacharek et al., 2002). Interestingly, this increase in spontaneous activity, i.e. neural hyperactivity, is correlated with the strength of the behavioral signs of tinnitus in animal models (Kaltenbach et al., 2004). Furthermore, the hyperactivity is localized in those regions of the tonotopically organized DCN that are innervated by the damaged parts of the cochlea (Kaltenbach et al., 2002). Gao and colleagues (Gao et al., 2016) recently described changes in DCN fusiform cell spontaneous activity

after noise exposure that perfectly supports the proposed SR mechanism. In particular, the time course of spontaneous rate changes shows an almost complete loss of spontaneous activity immediately after loud sound exposure (as no SR is needed due to stimulation that is well above threshold), followed by an overcompensation of spontaneous rates to levels well above pre-exposition rates since SR is now used to compensate for acute hearing loss (Gao et al., 2016).

It is well known that the DCN receives not only auditory input from the cochlea, but also input from the somatosensory system (Ryugo et al., 2003; Shore & Zhou 2006; Wu et al., 2015), and that noise trauma alters long-term somatosensory-auditory processing in the DCN (Dehmel et al., 2008, 2012; Shore 2011; Wu et al., 2016), i.e. somatosensory projections are up-regulated after hearing loss (Zeng et al., 2012). In addition, DCN responses to somatosensory stimulation are enhanced after noise-induced hearing loss (Shore, 2011; Shore et al., 2008; Wu et al., 2016). Therefore, we previously proposed the possibility that the neural noise which is necessary for SR is injected into the auditory system via somatosensory projections to the DCN (Krauss et al., 2016, 2018, 2019b), and that these non-auditory projections into the DCN are the cause of the altered "spontaneous activity" within the DCN after hearing loss described previously (Gao et al., 2016). From an information processing point of view, somatosensory inputs are completely uncorrelated, i.e. have no mutual auditory information. Hence, these somatosensory inputs are perfectly suited to serve as a random signal, i.e. noise, in the context of SR, and this seems to be the reason why the auditory system does not generate the noise needed for SR itself.

Our idea that cross-modal SR, with cochlear inputs being the signal and somatosensory projections being the noise (Fig. 2), is a key processing principle of the auditory system and actually takes place in the DCN (Krauss et al., 2018) is supported by a large number of different findings. For instance, it is well known, that jaw movements lead to a modulation of subjective tinnitus loudness (Pinchoff et al., 1998). This may easily be explained within our framework, as jaw movements alter somatosensory input to the DCN: Since this somatosensory input corresponds to the noise for SR, auditory input to the DCN is modulated through this mechanism, and the altered noise level would then be perceived as modulated tinnitus (Krauss et al., 2016, 2018, 2019b). Along the same line, one may explain why both, the temporomandibular joint syndrome and whiplash, frequently cause so called somatic tinnitus (Levine, 1999; Shore et al., 2007).

Furthermore, the finding of Tang and Trussell that somatosensory input and hence tinnitus sensation may also be modified by serotonergic regulation of excitability of principal cells in the DCN (Tang & Trussell, 2015, 2017) supports the SR model. It even provides a mechanistic explanation of salicylate induced tinnitus, since salicylate affects DCN processing by disinhibition of somatosensory inputs (Koerber et al., 1966; Stolzberg et al., 2012). Thus, it increases the noise in the auditory system, which then may again be perceived as a phantom sound.

Finally, and maybe most remarkable, electro-tactile stimulation of finger tips, i.e. increased somatosensory input, significantly improves both, melody recognition (Huang et al., 2020) and speech recognition (Huang et al., 2017) in patients with

cochlear implants. Very recently, we were able to reproduce and mechanistically explain this finding, using a hybrid-computational model that exploits SR. The model consists of a cochlea model, a DCN model and an artificial deep neural network trained on a speech recognition task representing all further processing stages of the auditory pathway beyond the DCN. Simulated hearing loss, i.e. weakening the input from the cochlea model to the DCN model, reduced accuracy for speech recognition in the deep neural network, as expected. However, subsequent addition of noise, i.e. somatosensory input to the DCN model, results in an improved accuracy for speech recognition (Schilling et al., 2020).

3 Zwicker tone illusion

The Zwicker tone effect was discovered by Eberhard Zwicker in 1964 and is a temporal auditory phantom percept which was originally induced by the presentation of a 60 dB broadband noise with a spectral gap (notched noise) with a gap-width of half an octave (Zwicker, 1964). The Zwicker tone was described as "Negative Auditory After Image," although the underlying mechanisms generating an "After Image" are supposed to be different in the visual system. The Zwicker tone perception is not exclusively induced by a notched noise stimulus, but can also be caused by low-pass noise or white noise with a loud pure tone embedded (Fastl et al., 2001; Franosch et al., 2003).

Several models exist trying to explain the Zwicker tone percept. For example, Franosch and colleagues viewed the Zwicker tone as an asymmetric lateral inhibition effect along the auditory pathway (Franosch et al., 2003). In this view, the neurons in the DCN are disinhibited by surrounding neurons, which receive less stimulus driven activity due to the notch.

Another model suggested the Zwicker tone to be caused by a prediction error within the cortex in combination with an increased spontaneous rate of auditory pathway neurons at frequency ranges deprived by the notch within the presented broadband noise (Hullfish et al., 2019). However, these models have certain shortcomings such as they do not account for all properties of Zwicker tone percepts (described in the following) or do not describe the effect on a neuronal network level.

It has previously been proposed that the Zwicker tone and tinnitus and thus also the neural mechanisms of these two auditory phantom perceptions are closely connected (Hoke et al., 1996; Lummis and Guttmann, 1972; Mohan et al., 2020), and a number of findings support this assumption: For example, Parra and Pearlmutter were able to show that people with a tinnitus percept are also more likely to perceive a Zwicker tone percept (Parra & Pearlmutter, 2007). Additionally, Wiegrebe and coworkers showed that the presence of a Zwicker tone leads to decreased auditory thresholds of 13 dB even in normal hearing subjects (Norena et al. 1999; Wiegrebe et al., 1996), a finding which may easily be explained within our above described model of SR, since a similar effect can be observed in tinnitus patients (Gollnast et al., 2017; Krauss et al. 2016) who have improved hearing thresholds

in comparison to patients without tinnitus, at least within frequency ranges below 3 kHz. In this context, psychoacoustic experiments revealed that notched noise presentation leads to higher sensitivity to tones embedded in noise (Zhou et al., 2010).

Next, human studies using MEG showed that Zwicker tone perception correlates with a reduced alpha activity (Leske et al., 2014) in the auditory cortex. Interestingly, the effect of reduced alpha activity is also correlated to tinnitus perception (Weisz et al. 2007, 2011).

Furthermore, in most models tinnitus is supposed to be caused by hearing loss (Moffat et al., 2009) through e.g. cochlea damage or hidden hearing loss which cannot be detected by pure-tone audiograms but is characterized by a deafferentation of the inner hair cells (Liberman & Liberman, 2015; Paul et al., 2017). Analogously, the induction of the Zwicker tone through notched noise can be viewed as a deprivation of certain inner hair cells, that is, a temporary and reversible hearing loss (Hullfish et al., 2019).

These observations and resemblances support the view that the neural mechanisms of Zwicker tone and acute tinnitus are similar and that therefore the Zwicker tone may be a good model for tinnitus (Franosch et al. 2003; Hullfish et al., 2019; Krauss et al. 2018; Norena et al., 1999, 2000, 2002; Wrzosek et al., 2017). As a result, the investigation of the Zwicker tone has recently attracted further attention. Norena & Eggermont showed that Zwicker tone related neuronal activity changes can be observed on time scales in the range of seconds (Norena & Eggermont, 2003). In particular, cats were implanted with multi-electrode arrays and notched noise stimuli of 1 s duration were presented. It could be shown that neurons in the auditory cortex representing frequencies within the range of the notch show increased firing rates after notched noise presentation (Norena & Eggermont, 2003). This result indicates that the Zwicker tone is correlated with a hyperactivity of neurons along the complete auditory pathway that represent the frequency notch, although to our knowledge systematic studies of activity along the auditory pathway in animals during Zwicker tone induction are missing.

Despite all these similarities between the Zwicker tone and acute tinnitus, there are only few mechanistic explanation approaches on a neural network level (Okamoto et al., 2005). Our stochastic resonance model (Krauss et al., 2016, see above) provides such a mechanistic explanation of Zwicker tone percepts. As stated above the presentation of a notched noise stimulus can be viewed as temporary hearing loss or deprivation of inner hair cells located within the frequency notch within the tonotopic gradient (Hullfish et al., 2019; Krauss et al., 2018). According to our model, this reduced input would cause SR within the auditory system to restore hearing by optimizing information transmission at the level of the DCN via increased neuronal noise (as described above). This increase of the neural noise would take place within the frequency channels of the spectral notch, leading to a hyperactivity of the respective neurons in the DCN (Krauss et al., 2016). This hyperactivity is transmitted along the auditory pathway and causes a Zwicker tone percept at the cortical level.

Our explanation is supported by the observation that notched noise stimulation leads to hyperactivity of auditory cortex neurons representing the notch frequency

(cf. Norena & Eggermont, 2003) via disinhibition (cf. Weisz et al., 2007, 2011). Furthermore, only the SR mechanism may explain improved hearing thresholds for frequencies near the Zwicker tone frequency during Zwicker tone perception (cf. Norena et al. 1999; Wiegrebe et al., 1996): internal noise from the somatosensory system is increased in the deprived frequency ranges (notch frequency range) in order to compensate for reduced auditory input by means of SR. This, in turn, leads as a side effect to improved hearing thresholds for neighboring frequencies above and below the notch. Additionally, the SR feedback control circuit (Fig. 2) operates on time scales in the range of or below a second and thus fits to the observation of Zwicker tone related hyperactivity after 1 s of notched noise presentation (Norena & Eggermont, 2003).

According to our model, the increased neural noise to the DCN which is necessary for SR is supposed to originate from the somatosensory system (Krauss et al., 2016, 2018, 2019b). In analogy to the afore mentioned phenomenon of tinnitus modulation by voluntary jaw movements, our model also predicts a modulation of the Zwicker tone perception by somatosensory stimulation. It has indeed been reported that transcutaneous electrical stimulation has an effect on Zwicker tone perception (Ueberfuhr et al., 2017).

4 Residual inhibition

In 1971 Feldmann found that the presentation of acoustic noise leads to a suppression of the tinnitus precept after noise offset (Feldmann, 1971), for approximately 1 min (Roberts, 2007; Roberts et al., 2006). This effect was named Residual Inhibition (RI; Henry & Meikle, 2000; Vernon, 1977).

RI should not be mixed up with tinnitus masking, where tinnitus is perceived less intense as it is masked by a noise of similar frequency range (Hazell & Wood, 1981; Terry et al., 1983). In contrast, the presentation of masking noise causes RI *after* the end of noise presentation. As RI is a technique to temporarily modulate the tinnitus percept, it is a potential target for experimental studies on tinnitus mechanisms (Deklerck et al., 2019).

Interestingly, it was reported that RI works best when the masking noise covers the range of the hearing loss of the subjects and is related to the tinnitus pitch (Roberts et al., 2006, 2008). The cause of the suppression of the tinnitus percept during RI has been discussed to be a decreased spontaneous neural activity after masking noise offset (Galazyuk et al., 2017). This is in line with the explanation that there is a neural adaptation along the auditory pathway induced by the noise presentation (Fournier et al., 2018).

These findings emphasize the idea that spontaneous activity of spiking neurons or in other words internally generated neural noise are crucial for processing of acoustic stimuli along the auditory pathway (Galazyuk et al., 2019). This internal noise is suppressed after the presentation of external acoustic noise. To understand the basic neural mechanisms of RI as well as auditory phantom perception, it is crucial to gain a better understanding of how the neural noise contributes to auditory processing.

The idea that the neural system exploits the effect of SR to improve hearing (Krauss et al., 2016, 2018, 2019b) provides a putative explanation for the effect of RI. As described above, tinnitus is potentially induced by the deprivation of neurons along the auditory pathway in tonotopic regions where a cochlea damage occurred. Thus, the auditory system tries to compensate for this deprivation, i.e. hearing loss, by adding internally generated neural noise. This internally generated noise potentially produced by the somatosensory system and fed to the DCN is propagated along the auditory pathway to the cortex, where it is perceived as auditory phantom percept. RI is potentially the consequence of replacing internally generated neural noise by external acoustic noise. In this view, the external noise would replace the internal noise, thereby causing its downregulation and thus suppression of the tinnitus percept as already described in previous publications (Krauss et al., 2016, 2019b).

According to our model, the optimal noise is tuned and controlled on time scales of seconds via a control circuit (Krauss et al., 2016; Fig. 2). From this point of view, Zwicker tone and tinnitus are basically the same phenomenon, but on different time scales. Furthermore, the proposed control circuit would work inversely for Zwicker tone and RI. Whereas, the Zwicker tone corresponds to an upregulation of internal neural noise caused by a reduced auditory input (i.e. the notch), RI in contrast corresponds to a downregulation of internal noise, due to increased auditory input (i.e. external acoustic noise). Thus, both phenomena can be considered to be opposite effects that may be explained by exactly the same neural control circuitry proposed by our SR model. To put it in a slogan, the SR model of auditory processing suggests that "RI can be interpreted as an inverse Zwicker tone illusion."

5 Summary and discussion

In summary, our SR model provides a unified explanation for the induction of acute subjective tinnitus, Zwicker tone, and RI. The total duration these phenomena are perceived differs greatly, e.g. the Zwicker tone lasts a few seconds, residual inhibition a few minutes, and tinnitus might even last decades. However, the time scales on which these apparently different perceptions can be induced (e.g. the Zwicker tone, Norena & Eggermont, 2003), or reduced (e.g. tinnitus removal by hearing aids or cochlear implants, McNeill et al., 2012; Ito & Sakakihara, 1994; Baguley & Atlas, 2007), are within a narrow range of some seconds. This indicates that these phenomena cannot be exclusively explained by brain plasticity, which takes place on much longer time scales. The SR model, describing tinnitus as a side effect of the neural system trying to optimize information transmission after hearing loss by exploiting the SR effect, would offer an explanation of how these phantom perceptions can be induced or suppressed so quickly. Thus, the neural system does not need any plasticity in the first place as the SR mechanism is optimized by a simple control circuit (Krauss et al., 2016; Fig. 2).

One may argue that the advantage of the sensory system might be close to zero in individuals suffering from extreme hearing loss or deafness and ask why the injected

somatosensory noise apparently stays at a level that bears no benefit but rather evokes a percept that induces stress for the individual but comes without meaningful information. We argue that the knowledge, that this perception is actually a phantom perception without any physical source in the environment, is only available at the highest processing stages in the brain associated with conscious perception. In contrast, the early processing stages within the auditory pathway, i.e. the DCN, have no access to this knowledge, hence from the point of view of the DCN, a "pure tone" always contains the same amount of information whether its source is actually in the environment or not. Our proposed feedback-loop for the adjustment of noise intensity to maintain optimal information processing is comparable to a reflex arc in the motor system, but without any top-down regulation. Hence, the noise amplification is not readapted, since this would require both, knowledge about the phantom perception, which is only available to higher processing stages, and top-down connections from these higher processing stages to the DCN. Furthermore, results from another study of our group suggest that the information benefit (in this case, accuracy improvement in a speech recognition task) as a function of noise intensity may show, under certain conditions, a second maximum besides the global maximum (Schilling et al., 2020). Therefore, it seems possible that the noise adjusting feedback loop of the auditory system gets "trapped" in this side maximum.

We speculate that in subjects, where the Zwicker tone can be induced by short noise presentation the RI effect should vanish more quickly, because the tuning of the optimal noise level works faster in certain subjects and thus the downregulated neural noise during RI is quickly re-increased. On the other hand, the Zwicker tone is induced faster as the neural noise is quickly upregulated when notched noise is presented. Thus, the duration of notched noise needed to induce the Zwicker tone could potentially correlate with the duration of the RI effect. This would be only the case, if both effects were produced by the same SR control circuit in the DCN (Fig. 2), which could be a characteristic feature of different individuals. The characteristic parameter of this control circuit is the time needed for controlling the noise amplitude.

This is a testable hypothesis derived from the SR model, which has to be verified or falsified in future studies.

However, it is obvious that the SR model has some limitations, such as that -in contrast to homeostatic plasticity models- it does not predict massive structural and functional changes (cf. Noreña, 2011) along the auditory pathway, which is indeed found in several studies (Li et al., 2015; Singer et al., 2013; Yang et al., 2011). These findings are supported by computational models demonstrating the influence of this plasticity (Nagashino et al., 2012; Schaette & Kempter, 2006).

Additionally, our model does not address the question why not all people with hearing loss perceive or even suffer from tinnitus. The influence of stress (Mazurek et al., 2012, 2015) and psychological burden (Landgrebe & Langguth 2011; Langguth et al., 2007, 2011) on tinnitus percepts was shown in several studies. Furthermore, the model does not differentiate between chronic and acute tinnitus.

Despite these limitations, we are convinced that we now have the knowledge to draw a complete picture in the light of preceding studies. Figs. 3 and 4 provide an

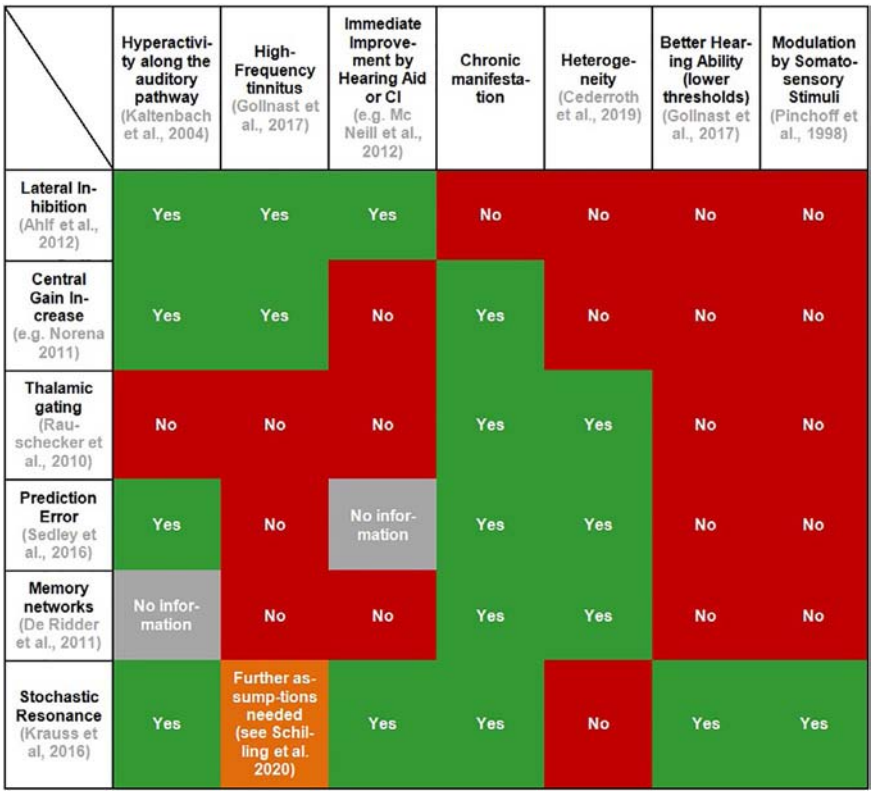

FIG. 3

Explanatory power of different models of tinnitus development. The figure summarizes different models of tinnitus development (rows) and how these models fit to certain observations (columns). For each model and effect, one exemplary paper is cited (e.g. Cederroth et al., 2019).

overview of the main models and their explanatory power for tinnitus development and Zwicker tone perception. The different models work on different time scales, as well as in different brain areas, as illustrated in Fig. 5.

Our SR model provides a mechanistic explanation of the initial cause ("the first seconds") leading to the induction of tinnitus after e.g. a loud acoustic noise presentation, the induction of the Zwicker tone illusion by notched noise, or the suppression of the tinnitus perception by acoustic noise presentation (i.e., residual inhibition). As mentioned above, these phenomena occur within seconds, and thus cannot be explained by any of the models based on brain plasticity. However, as described above, neural plasticity occurs along the auditory pathway (Li et al., 2015; Singer et al., 2013; Yang et al., 2011), and very probably contributes to chronic manifestation of tinnitus, yet after and on top of the initial induction caused by SR.

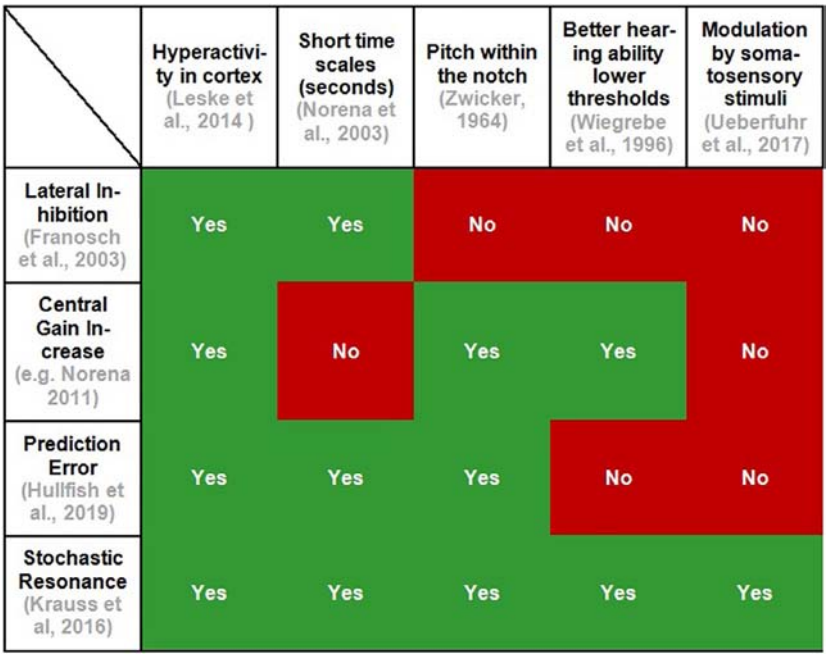

FIG. 4

Explanatory power of different models of the Zwicker tone illusion. The figure summarizes different models of the Zwicker tone illusion (rows) and how these models fit to certain observations (columns). For each model and effect, one exemplary paper is cited.

Furthermore, it is still unclear why the gating function of the thalamus does not prevent the neural hyperactivity from being directly transmitted to the cortex as it does for other unwanted permanent stimuli (McCormick & Bal, 1994). This effect could be explained by the model of Rauschecker and coworkers (Rauschecker et al., 2010). There, the auditory input can be canceled out by the medial geniculate nucleus within the thalamus. This noise cancellation function can be modulated by the limbic system especially the nucleus accumbens, which is indirectly connected to the medial geniculate nucleus. A breakdown of this system impairs the gating function of the medial geniculate nucleus (Rauschecker et al., 2010) and thus brings the neural hyperactivity to consciousness.

De Ridder and coworkers go even one step further and assume a conscious tinnitus percept to be a consequence of different overlapping brain networks including prefrontal areas as well as brain structures responsible for emotional labeling of certain memories such as the amygdala. Thus, learning effects are involved, which generate a connection of the phantom percept and distress (De Ridder et al., 2011). Unfortunately, this model does not provide mechanistic explanations at a neural network level, but it explains the involvement of different brain structures. Nevertheless, the model could provide an explanation why not every hearing loss causes tinnitus, and why not

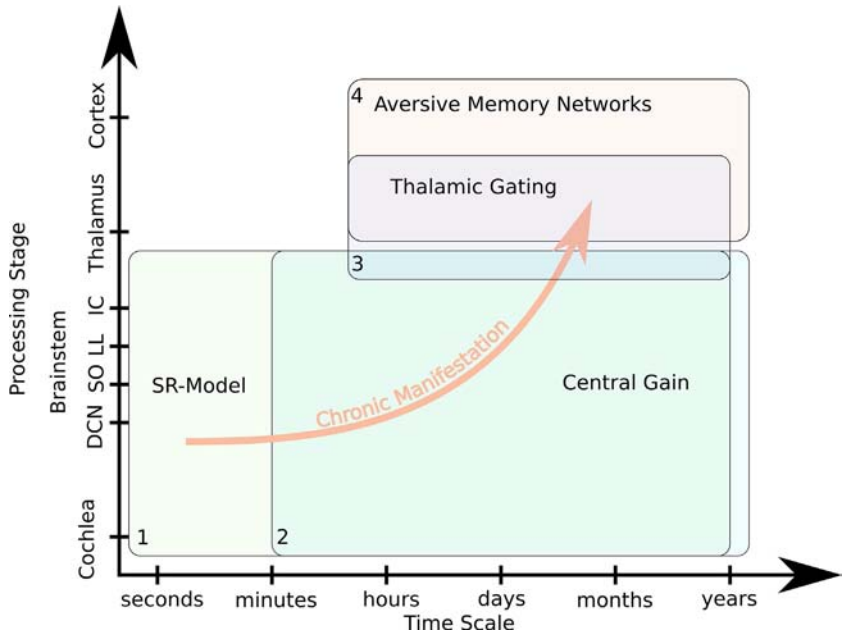

FIG. 5

The space of tinnitus models. Models of tinnitus development can be defined at different levels of description and can vary in time scale of the explained observations (horizontal axis) and in proposed anatomical substrate, i.e. processing stage (vertical axis). The SR model fills the "missing gap" in time scales of minutes and seconds.

everyone perceiving tinnitus also suffers from it. Individual memories and neuronal pathways could lead to different effects in different subjects.

Rather than mutually excluding each other as claimed by Sedley and coworkers (Sedley et al., 2016), the described models complement each other and draw a complete and consistent image of tinnitus development, its chronic manifestation, and heterogeneity. Furthermore, mechanistic explanations for RI, Zwicker tone, and better hearing thresholds of tinnitus patients compared to patients without tinnitus (Gollnast et al., 2017; Krauss et al., 2016) support the model.

Acknowledgments

This work was funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation): grant KR5148/2-1 to PK—project number 436456810, and grant SCHU1272/12-1 to HS—project number 332767752, and the Emergent Talents Initiative (ETI) of the University Erlangen-Nuremberg (grant 2019/2-Phil-01 to PK), and the Interdisciplinary Center for Clinical Research (IZKF) at the University Hospital of the University Erlangen-Nuremberg (grant ELAN-17-12-27-1-Schilling to AS).

We thank the reviewers for their valuable comments.

References

Ahlf, S., Tziridis, K., Korn, S., Strohmeyer, I., Schulze, H., 2012. Predisposition for and prevention of subjective tinnitus development. PLoS One 7 (10), e44519.

Aihara, T., Kitajo, K., Nozaki, D., Yamamoto, Y., 2008. Internal noise determines external stochastic resonance in visual perception. Vis. Res. 48 (14), 1569–1573.

Baguley, D.M., Atlas, M.D., 2007. Cochlear implants and tinnitus. Prog. Brain Res. 166, 347–355.

Benzi, R., Sutera, A., Vulpiani, A., 1981. The mechanism of stochastic resonance. J. Phys. A Math. Gen. 14 (11), L453.

Cederroth, C.R., Gallus, S., Hall, D.A., Kleinjung, T., Langguth, B., Maruotti, A., … Searchfield, G., 2019. Towards an understanding of tinnitus heterogeneity. Front. Aging Neurosci. 11, 53.

Chandrasekharan, S., Lebiere, C., Stewart, T.C., West, R.L., 2005. Stochastic resonance in human cognition: ACT-R versus game theory, associative neural networks, recursive neural networks, q-learning, and humans. In: Proceedings of the Annual Meeting of the Cognitive Science Society (Vol. 27, No. 27).

Collins, J.J., Imhoff, T.T., Grigg, P., 1996. Noise-enhanced tactile sensation. Nature 383, 770.

De Ridder, D., Elgoyhen, A.B., Romo, R., Langguth, B., 2011. Phantom percepts: tinnitus and pain as persisting aversive memory networks. Proc. Natl. Acad. Sci. 108 (20), 8075–8080.

Dehmel, S., Cui, Y.L., Shore, S.E., 2008. Cross-modal interactions of auditory and somatic inputs in the brainstem and midbrain and their imbalance in tinnitus and deafness. Am. J. Audiol. 17, S193–S209.

Dehmel, S., Pradhan, S., Koehler, S., Bledsoe, S., Shore, S., 2012. Noise overexposure alters long-term somatosensory-auditory processing in the dorsal cochlear nucleus—possible basis for tinnitus-related hyperactivity? J. Neurosci. 32 (5), 1660–1671.

Deklerck, A.N., Degeest, S., Dhooge, I.J., Keppler, H., 2019. Test–retest reproducibility of response duration in tinnitus patients with positive residual inhibition. J. Speech Lang. Hear. Res. 62 (9), 3531–3544.

Douglass, J.K., Wilkens, L., Pantazelou, E., Moss, F., 1993. Noise enhancement of information transfer in crayfish mechanoreceptors by stochastic resonance. Nature 365 (6444), 337–340.

Faisal, A.A., Selen, L.P., Wolpert, D.M., 2008. Noise in the nervous system. Nat. Rev. Neurosci. 9 (4), 292–303.

Fastl, H., Patsouras, D., Franosch, M., van Hemmen, L., 2001. Zwicker-tones for pure tone plus bandlimited noise. In: Proceedings of the 12th International Symposium on Hearing, Physiological and Psychophysical Bases of Auditory, pp. 67–74.

Feldmann, H., 1971. Homolateral and contralateral masking of tinnitus by noise-bands and by pure tones. Audiology 10 (3), 138–144.

Fournier, P., Cuvillier, A.F., Gallego, S., Paolino, F., Paolino, M., Quemar, A., … Norena, A., 2018. A new method for assessing masking and residual inhibition of tinnitus. Trends Hear. 22, 2331216518769996.

Franosch, J.M.P., Kempter, R., Fastl, H., van Hemmen, J.L., 2003. Zwicker tone illusion and noise reduction in the auditory system. Phys. Rev. Lett. 90 (17), 178103.

Galazyuk, A.V., Voytenko, S.V., Longenecker, R.J., 2017. Long-lasting forward suppression of spontaneous firing in auditory neurons: implication to the residual inhibition of tinnitus. J. Assoc. Res. Otolaryngol. 18 (2), 343–353.

Galazyuk, A.V., Longenecker, R.J., Voytenko, S.V., Kristaponyte, I., Nelson, G.L., 2019. Residual inhibition: from the putative mechanisms to potential tinnitus treatment. Hear. Res. 375, 1–13.

Gammaitoni, L., Hänggi, P., Jung, P., Marchesoni, F., 1998. Stochastic resonance. Rev. Mod. Phys. 70 (1), 223.
Gao, Y., Manzoor, N., Kaltenbach, J.A., 2016. Evidence of activity-dependent plasticity in the dorsal cochlear nucleus, in vivo, induced by brief sound exposure. Hear. Res. 341, 31–42.
Gerum, R.C., Rahlfs, H., Streb, M., Krauss, P., Grimm, J., Metzner, C., … Schilling, A., 2019. Open (G) PIAS: an open-source solution for the construction of a high-precision acoustic startle response setup for tinnitus screening and threshold estimation in rodents. Front. Behav. Neurosci. 13, 140.
Gluckman, B.J., Netoff, T.I., Neel, E.J., Ditto, W.L., Spano, M.L., Schiff, S.J., 1996. Stochastic resonance in a neuronal network from mammalian brain. Phys. Rev. Lett. 77 (19), 4098.
Gollnast, D., Tziridis, K., Krauss, P., Schilling, A., Hoppe, U., Schulze, H., 2017. Analysis of audiometric differences of patients with and without tinnitus in a large clinical database. Front. Neurol. 8, 31.
Hänggi, P., 2002. Stochastic resonance in biology how noise can enhance detection of weak signals and help improve biological information processing. ChemPhysChem 3 (3), 285–290.
Hazell, J.W.P., Wood, S.M., 1981. Tinnitus masking-a significant contribution to tinnitus management. Br. J. Audiol. 15 (4), 223–230.
Hébert, S., Fournier, P., Noreña, A., 2013. The auditory sensitivity is increased in tinnitus ears. J. Neurosci. 33 (6), 2356–2364.
Heller, A.J., 2003. Classification and epidemiology of tinnitus. Otolaryngol. Clin. N. Am. 36 (2), 239–248.
Henry, J.A., Meikle, M.B., 2000. Psychoacoustic measures of tinnitus. J. Am. Acad. Audiol. 11 (3), 138–155.
Hoke, E.S., Hoke, M., Ross, B., 1996. Neurophysiological correlate of the auditory after-image ('ZwickerTone'). Audiol. Neurootol. 1 (3), 161–174.
Huang, J., Sheffield, B., Lin, P., Zeng, F.G., 2017. Electro-tactile stimulation enhances cochlear implant speech recognition in noise. Sci. Rep. 7 (1), 1–5.
Huang, J., Lu, T., Sheffield, B., Zeng, F.G., 2020. Electro-tactile stimulation enhances cochlear-implant melody recognition: effects of rhythm and musical training. Ear Hear. 41 (1), 106–113.
Hullfish, J., Sedley, W., Vanneste, S., 2019. Prediction and perception: insights for (and from) tinnitus. Neurosci. Biobehav. Rev. 102, 1–12.
Ito, J., Sakakihara, J., 1994. Suppression of tinnitus by cochlear implantation. Am. J. Otolaryngol. 15 (2), 145–148.
Kaltenbach, J.A., Afman, C.E., 2000. Hyperactivity in the dorsal cochlear nucleus after intense sound exposure and its resemblance to tone-evoked activity: a physiological model for tinnitus. Hear. Res. 140 (1–2), 165–172.
Kaltenbach, J.A., Godfrey, D.A., Neumann, J.B., McCaslin, D.L., Afman, C.E., Zhang, J., 1998. Changes in spontaneous neural activity in the dorsal cochlear nucleus following exposure to intense sound: relation to threshold shift. Hear. Res. 124 (1–2), 78–84.
Kaltenbach, J.A., Rachel, J.D., Mathog, T.A., Zhang, J., Falzarano, P.R., Lewandowski, M., 2002. Cisplatin-induced hyperactivity in the dorsal cochlear nucleus and its relation to outer hair cell loss: relevance to tinnitus. J. Neurophysiol. 88 (2), 699–714.
Kaltenbach, J.A., Zacharek, M.A., Zhang, J., Frederick, S., 2004. Activity in the dorsal cochlear nucleus of hamsters previously tested for tinnitus following intense tone exposure. Neurosci. Lett. 355 (1–2), 121–125.
Kitajo, K., Nozaki, D., Ward, L.M., Yamamoto, Y., 2003. Behavioral stochastic resonance within the human brain. Phys. Rev. Lett. 90 (21), 218103.

Koerber, K.C., Pfeiffer, R.R., Warr, W.B., Kiang, N.Y.S., 1966. Spontaneous spike discharges from single units in the cochlear nucleus after destruction of the cochlea. Exp. Neurol. 16 (2), 119–130.

König, O., Schaette, R., Kempter, R., Gross, M., 2006. Course of hearing loss and occurrence of tinnitus. Hear. Res. 221 (1–2), 59–64.

Kosko, B., Mitaim, S., 2003. Stochastic resonance in noisy threshold neurons. Neural Netw. 16 (5–6), 755–761.

Krauss, P., Tziridis, K., Metzner, C., Schilling, A., Hoppe, U., Schulze, H., 2016. Stochastic resonance controlled upregulation of internal noise after hearing loss as a putative cause of tinnitus-related neuronal hyperactivity. Front. Neurosci. 10, 597.

Krauss, P., Metzner, C., Schilling, A., Schütz, C., Tziridis, K., Fabry, B., Schulze, H., 2017. Adaptive stochastic resonance for unknown and variable input signals. Sci. Rep. 7 (1), 1–8.

Krauss, P., Tziridis, K., Schilling, A., Schulze, H., 2018. Cross-modal stochastic resonance as a universal principle to enhance sensory processing. Front. Neurosci. 12, 578.

Krauss, P., Schilling, A., Tziridis, K., Schulze, H., 2019a. Models of tinnitus development: from cochlea to cortex. HNO 67, 172–177.

Krauss, P., Prebeck, K., Schilling, A., Metzner, C., 2019b. "Recurrence resonance" in three-neuron motifs. Front. Comput. Neurosci. 13, 64.

Landgrebe, M., Langguth, B., 2011. Tinnitus and psychiatric co-morbidity. In: Møller, A.R., Langguth, B., DeRidder, D., Kleinjung, T. (Eds.), Textbook of Tinnitus. Springer, New York, NY, pp. 491–492.

Langguth, B., Kleinjung, T., Fischer, B., Hajak, G., Eichhammer, P.S.P.G., Sand, P.G., 2007. Tinnitus severity, depression, and the big five personality traits. Prog. Brain Res. 166, 221–225.

Langguth, B., Landgrebe, M., Kleinjung, T., Sand, G.P., Hajak, G., 2011. Tinnitus and depression. World J. Biol. Psychiatry 12 (7), 489–500.

Leske, S., Tse, A., Oosterhof, N.N., Hartmann, T., Müller, N., Keil, J., Weisz, N., 2014. The strength of alpha and beta oscillations parametrically scale with the strength of an illusory auditory percept. NeuroImage 88, 69–78.

Levine, R.A., 1999. Somatic (craniocervical) tinnitus and the dorsal cochlear nucleus hypothesis. Am. J. Otolaryngol. 20 (6), 351–362.

Li, S., Kalappa, B.I., Tzounopoulos, T., 2015. Noise-induced plasticity of KCNQ2/3 and HCN channels underlies vulnerability and resilience to tinnitus. elife 4, e07242.

Liberman, L.D., Liberman, M.C., 2015. Dynamics of cochlear synaptopathy after acoustic overexposure. J. Assoc. Res. Otolaryngol. 16 (2), 205–219.

Lummis, R.C., Guttman, N., 1972. Exploratory studies of Zwicker's "negative afterimage" in hearing. J. Acoust. Soc. Am. 51 (6B), 1930–1944.

Mazurek, B., Haupt, H., Olze, H., Szczepek, A.J., 2012. Stress and tinnitus—from bedside to bench and back. Front. Syst. Neurosci. 6, 47.

Mazurek, B., Szczepek, A.J., Hebert, S., 2015. Stress and tinnitus. HNO 63 (4), 258–265.

McCormick, D.A., Bal, T., 1994. Sensory gating mechanisms of the thalamus. Curr. Opin. Neurobiol. 4 (4), 550–556.

McDonnell, M.D., Abbott, D., 2009. What is stochastic resonance? Definitions, misconceptions, debates, and its relevance to biology. PLoS Comput. Biol. 5 (5), e1000348.

McNeill, C., Távora-Vieira, D., Alnafjan, F., Searchfield, G.D., Welch, D., 2012. Tinnitus pitch, masking, and the effectiveness of hearing aids for tinnitus therapy. Int. J. Audiol. 51 (12), 914–919.

Mino, H., 2014. The effects of spontaneous random activity on information transmission in an auditory brain stem neuron model. Entropy 16 (12), 6654–6666.

Mitaim, S., Kosko, B., 1998. Adaptive stochastic resonance. Proc. IEEE 86 (11), 2152–2183.
Mitaim, S., Kosko, B., 2004. Adaptive stochastic resonance in noisy neurons based on mutual information. IEEE Trans. Neural Netw. 15 (6), 1526–1540.
Moffat, G., Adjout, K., Gallego, S., Thai-Van, H., Collet, L., Norena, A.J., 2009. Effects of hearing aid fitting on the perceptual characteristics of tinnitus. Hear. Res. 254 (1–2), 82–91.
Mohan, A., Bhamoo, N., Riquelme, J.S., Long, S., Norena, A., Vanneste, S., 2020. Investigating functional changes in the brain to intermittently induced auditory illusions and its relevance to chronic tinnitus. Hum. Brain Mapp. 41, 1819–1832.
Moss, F., Ward, L.M., Sannita, W.G., 2004. Stochastic resonance and sensory information processing: a tutorial and review of application. Clin. Neurophysiol. 115 (2), 267–281.
Nagashino, H., Kinouchi, Y., Danesh, A.A., Pandya, A.S., 2012. A neuronal network model with homeostatic plasticity for tinnitus generation and its management by sound therapy. In: 2012 IEEE-EMBS Conference on Biomedical Engineering and Sciences. IEEE, pp. 706–711.
Nelson, J.J., Chen, K., 2004. The relationship of tinnitus, hyperacusis, and hearing loss. Ear Nose Throat J. 83 (7), 472–476.
Noreña, A.J., 2011. An integrative model of tinnitus based on a central gain controlling neural sensitivity. Neurosci. Biobehav. Rev. 35 (5), 1089–1109.
Norena, A.J., Eggermont, J.J., 2003. Neural correlates of an auditory afterimage in primary auditory cortex. J. Assoc. Res. Otolaryngol. 4 (3), 312–328.
Norena, A., Micheyl, C., Chéry-Croze, S., 1999. The Zwicker tone (ZT) as a model of phantom auditory perception. In: Sixth International Tinnitus Seminar, 429.
Norena, A., Micheyl, C., Chery-Croze, S., 2000. An auditory negative after-image as a human model of tinnitus. Hear. Res. 149 (1–2), 24–32.
Norena, A., Micheyl, C., Garnier, S., Chery-croze, S., 2002. Loudness changes associated with the perception of an auditory after-image: cambios en la intensidad asociados a la percepción de una imagen post-auditiva. Int. J. Audiol. 41 (3), 202–207.
Nozaki, D., Mar, D.J., Grigg, P., Collins, J.J., 1999. Effects of colored noise on stochastic resonance in sensory neurons. Phys. Rev. Lett. 82 (11), 2402.
Okamoto, H., Kakigi, R., Gunji, A., Kubo, T., Pantev, C., 2005. The dependence of the auditory evoked N1m decrement on the bandwidth of preceding notch-filtered noise. Eur. J. Neurosci. 21 (7), 1957–1961.
Parra, L.C., Pearlmutter, B.A., 2007. Illusory percepts from auditory adaptation. J. Acoust. Soc. Am. 121 (3), 1632–1641.
Paul, B.T., Bruce, I.C., Roberts, L.E., 2017. Evidence that hidden hearing loss underlies amplitude modulation encoding deficits in individuals with and without tinnitus. Hear. Res. 344, 170–182.
Pikovsky, A.S., Kurths, J., 1997. Coherence resonance in a noise-driven excitable system. Phys. Rev. Lett. 78 (5), 775.
Pinchoff, R.J., Burkard, R.F., Salvi, R.J., Coad, M.L., Lockwood, A.H., 1998. Modulation of tinnitus by voluntary jaw movements. Am. J. Otol. 19 (6), 785–789.
Rauschecker, J.P., Leaver, A.M., Mühlau, M., 2010. Tuning out the noise: limbic-auditory interactions in tinnitus. Neuron 66 (6), 819–826.
Roberts, L.E., 2007. Residual inhibition. Prog. Brain Res. 166, 487–495.
Roberts, L.E., Moffat, G., Bosnyak, D.J., 2006. Residual inhibition functions in relation to tinnitus spectra and auditory threshold shift. Acta Oto-Laryngol. 126 (sup556), 27–33.
Roberts, L.E., Moffat, G., Baumann, M., Ward, L.M., Bosnyak, D.J., 2008. Residual inhibition functions overlap tinnitus spectra and the region of auditory threshold shift. J. Assoc. Res. Otolaryngol. 9 (4), 417–435.

Ryugo, D.K., Haenggeli, C.A., Doucet, J.R., 2003. Multimodal inputs to the granule cell domain of the cochlear nucleus. Exp. Brain Res. 153 (4), 477–485.

Schaette, R., Kempter, R., 2006. Development of tinnitus-related neuronal hyperactivity through homeostatic plasticity after hearing loss: a computational model. Eur. J. Neurosci. 23 (11), 3124–3138.

Schaette, R., McAlpine, D., 2011. Tinnitus with a normal audiogram: physiological evidence for hidden hearing loss and computational model. J. Neurosci. 31 (38), 13452–13457.

Schilling, A., Krauss, P., Gerum, R., Metzner, C., Tziridis, K., Schulze, H., 2017. A new statistical approach for the evaluation of gap-prepulse inhibition of the acoustic startle reflex (GPIAS) for tinnitus assessment. Front. Behav. Neurosci. 11, 198.

Schilling, A., Gerum, R., Zankl, A., Schulze, H., Metzner, C., Krauss, P., 2020. Intrinsic noise improves speech recognition in a computational model of the auditory pathway. bioRxiv, 2020.03.16.993725. https://doi.org/10.1101/2020.03.16.993725.

Sedley, W., Friston, K.J., Gander, P.E., Kumar, S., Griffiths, T.D., 2016. An integrative tinnitus model based on sensory precision. Trends Neurosci. 39 (12), 799–812.

Shore, S.E., 2011. Plasticity of somatosensory inputs to the cochlear nucleus–implications for tinnitus. Hear. Res. 281 (1–2), 38–46.

Shore, S.E., Zhou, J., 2006. Somatosensory influence on the cochlear nucleus and beyond. Hear. Res. 216, 90–99.

Shore, S., Zhou, J., Koehler, S., 2007. Neural mechanisms underlying somatic tinnitus. Prog. Brain Res. 166, 107–548.

Shore, S.E., Koehler, S., Oldakowski, M., Hughes, L.F., Syed, S., 2008. Dorsal cochlear nucleus responses to somatosensory stimulation are enhanced after noise-induced hearing loss. Eur. J. Neurosci. 27 (1), 155–168.

Shore, S.E., Roberts, L.E., Langguth, B., 2016. Maladaptive plasticity in tinnitus—triggers, mechanisms and treatment. Nat. Rev. Neurol. 12 (3), 150.

Singer, W., Zuccotti, A., Jaumann, M., Lee, S.C., Panford-Walsh, R., Xiong, H., … Rohbock, K., 2013. Noise-induced inner hair cell ribbon loss disturbs central arc mobilization: a novel molecular paradigm for understanding tinnitus. Mol. Neurobiol. 47 (1), 261–279.

Stacey, W.C., Durand, D.M., 2001. Synaptic noise improves detection of subthreshold signals in hippocampal CA1 neurons. J. Neurophysiol. 86 (3), 1104–1112.

Stolzberg, D., Salvi, R.J., Allman, B.L., 2012. Salicylate toxicity model of tinnitus. Front. Syst. Neurosci. 6, 28.

Tang, Z.Q., Trussell, L.O., 2015. Serotonergic regulation of excitability of principal cells of the dorsal cochlear nucleus. J. Neurosci. 35 (11), 4540–4551.

Tang, Z.Q., Trussell, L.O., 2017. Serotonergic modulation of sensory representation in a central multisensory circuit is pathway specific. Cell Rep. 20 (8), 1844–1854.

Terry, A.M.P., Jones, D.M., Davis, B.R., Slater, R., 1983. Parametric studies of tinnitus masking and residual inhibition. Br. J. Audiol. 17 (4), 245–256.

Turner, J.G., Brozoski, T.J., Bauer, C.A., Parrish, J.L., Myers, K., Hughes, L.F., Caspary, D.M., 2006. Gap detection deficits in rats with tinnitus: a potential novel screening tool. Behav. Neurosci. 120 (1), 188.

Tziridis, K., Ahlf, S., Jeschke, M., Happel, M.F., Ohl, F.W., Schulze, H., 2015. Noise trauma induced neural plasticity throughout the auditory system of Mongolian gerbils: differences between tinnitus developing and non-developing animals. Front. Neurol. 6, 22.

Ueberfuhr, M.A., Braun, A., Wiegrebe, L., Grothe, B., Drexl, M., 2017. Modulation of auditory percepts by transcutaneous electrical stimulation. Hear. Res. 350, 235–243.

Usher, M., Feingold, M., 2000. Stochastic resonance in the speed of memory retrieval. Biol. Cybern. 83 (6), L011–L016.
Vernon, J., 1977. Attempts to relieve tinnitus. J. Am. Audiol. Soc. 2, 124–131.
Wang, J., Powers, N.L., Hofstetter, P., Trautwein, P., Ding, D., Salvi, R., 1997. Effects of selective inner hair cell loss on auditory nerve fiber threshold, tuning and spontaneous and driven discharge rate. Hear. Res. 107 (1–2), 67–82.
Ward, L.M., Neiman, A., Moss, F., 2002. Stochastic resonance in psychophysics and in animal behavior. Biol. Cybern. 87 (2), 91–101.
Weisz, N., Müller, S., Schlee, W., Dohrmann, K., Hartmann, T., Elbert, T., 2007. The neural code of auditory phantom perception. J. Neurosci. 27 (6), 1479–1484.
Weisz, N., Hartmann, T., Müller, N., Obleser, J., 2011. Alpha rhythms in audition: cognitive and clinical perspectives. Front. Psychol. 2, 73.
Wenning, G., Obermayer, K., 2003. Activity driven adaptive stochastic resonance. Phys. Rev. Lett. 90 (12), 120602.
Wiegrebe, L., Kössl, M., Schmidt, S., 1996. Auditory enhancement at the absolute threshold of hearing and its relationship to the Zwicker tone. Hear. Res. 100 (1–2), 171–180.
Wiesenfeld, K., Moss, F., 1995. Stochastic resonance and the benefits of noise: from ice ages to crayfish and SQUIDs. Nature 373 (6509), 33–36.
Wrzosek, M., Szymiec, E., Obrebowska, Z., Norena, A., 2017. Continuous Zwicker tone illusion imitates tonal tinnitus-could Zwicker tone generators imitate different types of hearing loss? J. Hear. Sci. 7 (2), 168.
Wu, C., Stefanescu, R.A., Martel, D.T., Shore, S.E., 2015. Listening to another sense: somatosensory integration in the auditory system. Cell Tissue Res. 361 (1), 233–250.
Wu, C., Stefanescu, R.A., Martel, D.T., Shore, S.E., 2016. Tinnitus: maladaptive auditory–somatosensory plasticity. Hear. Res. 334, 20–29.
Yang, S., Weiner, B.D., Zhang, L.S., Cho, S.J., Bao, S., 2011. Homeostatic plasticity drives tinnitus perception in an animal model. Proc. Natl. Acad. Sci. U. S. A. 108 (36), 14974–14979.
Zacharek, M.A., Kaltenbach, J.A., Mathog, T.A., Zhang, J., 2002. Effects of cochlear ablation on noise induced hyperactivity in the hamster dorsal cochlear nucleus: implications for the origin of noise induced tinnitus. Hear. Res. 172 (1–2), 137–144.
Zeng, C., Yang, Z., Shreve, L., Bledsoe, S., Shore, S., 2012. Somatosensory projections to cochlear nucleus are upregulated after unilateral deafness. J. Neurosci. 32 (45), 15791–15801.
Zhou, X., Henin, S., Thompson, S.E., Long, G.R., Parra, L.C., 2010. Sensitization to masked tones following notched-noise correlates with estimates of cochlear function using distortion product otoacoustic emissions. J. Acoust. Soc. Am. 127 (2), 970–976.
Zwicker, E., 1964. “Negative afterimage” in hearing. J. Acoust. Soc. Am. 36 (12), 2413–2415.