



# HHS Public Access

Author manuscript

*Curr Opin Physiol.* Author manuscript; available in PMC 2021 December 01.

Published in final edited form as:

*Curr Opin Physiol.* 2020 December ; 18: 123–129. doi:10.1016/j.cophys.2020.10.009.

## Tinnitus and hyperacusis: Central noise, gain and variance

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### Abstract

Tinnitus is a phantom auditory sensation in the absence of external sounds, while hyperacusis is an atypical sensitivity to external sounds that leads them to be perceived as abnormally loud or even painful. Both conditions may reflect the brain's over-compensation for reduced input from the ear. The present work differentiates between two compensation models: The additive central noise compensates for hearing loss and is likely to generate tinnitus, whereas the multiplicative central gain compensates for hidden hearing loss and is likely to generate hyperacusis. Importantly, both models predict increased variance in central representations of sounds, especially a nonlinear increase in variance by the central gain. The increased central variance limits the amount of central compensation and reduces temporal synchrony, which can explain the insufficient central gain reported in the literature. Future studies need to collect trial-by-trial firing variance data so that the present variance-based model can be falsified.

### Keywords

Central Variance; Central Noise; Central Gain; Temporal Coding; Dynamic Range Normalization

### Introduction

Tinnitus is a phantom perception of a sound in the absence of external sounds, whereas hyperacusis is an excessive response to external sounds [1]. Tinnitus affects 15% of the general population and is typically perceived as a ringing sensation in the ear or head. Individuals with hyperacusis cannot tolerate conventional loud sounds or even report painful responses to these sounds. At first glance, tinnitus and hyperacusis are opposites, but they are intertwined clinically. Nearly half of tinnitus sufferers report some degree of hyperacusis, while most hyperacusis sufferers have tinnitus [2].

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Conflict of interest statement

The author owns stock in Axonics, DiaNavi, Nurotron, Syntiant, Velox and Xense.

Hearing loss is a common and main risk factor for both conditions [3, 4]. Recent advances have broadened the definition of hearing loss, which traditionally was defined by elevated audiometric thresholds between 125 and 8000 Hz. A key advance is the discovery of “hidden” hearing loss, in which there is no elevation of audio metric thresholds but there is reduced auditory nerve activity due to cochlear synaptopathy and secondary nerve degeneration [5]. Although some individuals with tinnitus do not have any hearing loss, they may suffer from hidden hearing loss [6, 7]. Indeed, studies on tinnitus without hearing loss often found evidence for the presence of hidden hearing loss and its involvement in hyperacusis in humans [7-10] or animals [11-13]. The current view is that both tinnitus and hyperacusis are consequences of the central auditory system’s compensatory responses to the reduced peripheral input due to either overt or hidden hearing loss.

At present, the exact central compensatory mechanisms are not clear. Hearing loss causes massive changes in the central auditory system, from to notopic reorganization and hyperactivity to altered network connectivity within and beyond the auditory system [14-18]. Some of these central changes cause tinnitus and hyperacusis but others may not. For example, excessive to notopic reorganization was thought of as a main mechanism for tinnitus [19], but a recent brain imaging study found the opposite; only those hearing-impaired individuals who have incomplete tonotopic reorganization develop tinnitus [20]. In contrast, central hyperactivity has been consistently observed from the cochlear nucleus to the auditory cortex, evidenced by increased spontaneous firing rate or restored driven activity [21-26]. Because hearing loss actually reduces both spontaneous and driven activity in the auditory nerve fibers [27, 28], such central hyperactivity is considered to be the result of a compensatory response to hearing loss. Tinnitus and hyperacusis are likely a consequence of this central compensation or over-compensation [7, 29, 30]. In addition to the bottom-up compensatory mechanism, several top-down mechanisms such as noise cancellation, predictive errors or attention may influence the generation and behavior of tinnitus and hyperacusis [31-34].

The present work builds upon the previous suggestions that tinnitus is caused by increased central noise and hyperacusis by increased central gain [30]. Here I propose a third mechanism, namely central variance, which may affect the relative contributions of central noise and central gain to tinnitus and hyperacusis.

First consider what happens when the total central activity is the sum of compensatory additive central noise ( $N$ ) and driven activity ( $D$ ). Then the total mean activity is the sum of the two individual means:

$$\text{Mean}(N + D) = \text{Mean}(N) + \text{Mean}(D) \quad (1)$$

while the total variance is the sum of the two variances [p140 in 35]:

$$\text{Var}(N + D) = \text{Var}(N) + \text{Var}(D) \quad (2)$$

Alternatively, applying a gain ( $g$ ) to the driving activity results in a proportional increase in the total mean activity:

$$\text{Mean}(gD) = g\text{Mean}(D); \quad (3)$$

however, the total variance increases nonlinearly by the square of the gain [p106 in 35]:

$$\text{Var}(gD) = g^2\text{Var}(D) \quad (4)$$

Thus, increasing central noise and increasing central gain lead to different predictions for how central variance changes. The next section considers how these different effects on central variance may help explain tinnitus and hyperacusis.

### Tinnitus: Increased central noise and variance

Figure 1(a) shows schematically the effect of hearing loss on auditory nerve activity as a function of sound level (left panel) and time (right panel). Compared with the normal mean activity (blue lines), hearing loss elevates the hearing threshold (double-angled green line below the x-axis, left panel) and reduces the overall auditory nerve mean activity (solid green lines in both panels) [28]. To a first-order approximation [36], the firing variance is proportional to the mean firing rate (dashed lines, left panel; or amplitude fluctuations, right panel).

Figure 1(b) shows the effects of adding a central noise on loudness represented at a higher level of auditory processing, both as a function of sound level (left panel) and time (right panel). The additive central noise (represented by two upward angled black lines, left panel) restores normal loudness growth at high sound levels (solid orange sloping line, left panel) but raises the baseline loudness at and below threshold (solid orange horizontal line above “Tinnitus”, both panels). Similarly, the central noise increases the baseline variance (dashed orange horizontal line, left panel, and amplitude fluctuations above “Tinnitus”, right panel) but not the slope of the normal variance function (dashed blue line).

These schematical effects are consistent with behavioral observations that individuals with hearing loss have a normal slope of the loudness function but abnormally large loudness at the threshold [37]. In other words, the central noise compensates for hearing loss by restoring normal loudness growth above threshold, but generates tinnitus at or below the hearing threshold.

### Hyperacusis: Increased central gain and variance

Figure 2(a) shows a schematic similar to Figure 1(a), except for hidden hearing loss. Unlike in traditional hearing loss, hidden hearing loss does not elevate the hearing threshold, but instead produces a shallower-than-normal auditory nerve rate-level function (solid purple line=mean; dashed purple line=variance, left panel) and reduced activity (purple line, right panel).

Figure 2(b) shows the effects of increasing central gain on loudness as a function of sound level (left panel) and time (right panel). The multiplicative central gain (a factor of two in this case) restores mean normal loudness growth at all sound levels (solid diagonal red

line=solid blue line, left panel) but increases the amount of the central variance by a factor of four. As a result, the quadrupled variance produces hyperacusis at high sound levels (double-headed red line, left panel; and solid red lines outside the box reflecting amplitude fluctuations beyond normal loudness range, right panel).

### Central variance limits the amount of compensation

This analysis of a central noise model assumes that internal noise and driven activities are summed up in the central auditory system [38]. If the internal and driven activities are not additive but instead multiplicative [26], then the resulting variance can be 10-100 times larger than the individual variance, depending on the squared terms of both individual means and variances [39]. Similarly, if the actual central gain compensation involves a cascade of amplifiers [13, 40], then the central variance can grow geometrically. In reality, an individual may have mixed hearing loss, requiring both forms of compensation, which further exacerbate the central variance problem.

An inevitable consequence of the large central variance is a severe limitation on the amount of central compensation that can be accommodated. To minimize the likelihood of tinnitus and hyperacusis, neither the central noise nor the central gain would be expected to reach the level that restores the normal mean value. This lower-than-expected compensation limit is more pronounced for increases in central gain than for additive noise because the variance increases much more when the compensation is multiplicative rather than additive. Thus, it is not too surprising that recent studies found insufficient central gain because they all used the normal mean response as the criterion [41-44].

### Central variance reduces temporal synchrony

Considering how increased variance influences central representations reconciles other conflicting results in the literature. For example, early studies found a reduced auditory brainstem response for wave I but a normal or even increased wave V response in human tinnitus subjects with normal audiograms [7, 45]. Recent studies could not replicate these findings in a large cohort of similar human tinnitus subjects [44, 46] or in subjects with a history of noise exposure [47]. Instead, several studies found delayed auditory brainstem responses [48, 49].

The auditory brainstem response is determined by the total synchronized activity across all responding neurons [50, see their Fig. 13]. It is possible that early studies used subjects with a relatively small central gain while recent studies used subjects with a larger central gain. The linearly increasing gain cannot make up for the dys-synchrony caused by the nonlinearly increasing variance, such that a synchronized amplitude measure, like wave V, underestimates the true central gain. In this case, more dys-synchrony actually indicates larger gain. Indeed, there is evidence showing that temporal measures are more sensitive than amplitude measures in detecting hidden hearing loss in humans [51, 52]. Of course, single-unit recordings would not have this gain vs. variance dilemma, but at present no studies have reported trial-to-trial firing rate variance from single units.

## Dynamic range normalization

The central variance problem can be reduced by dynamic range normalization [53], which is widely used in the nervous system to adapt to external signals [54] and internal noise [55] in order to preserve stimulus sensitivity and prevent response saturation [56-59]. The neural system also needs to maintain the same average energy, e.g., the same average firing rate [60]. Activation of the fast-spiking auditory pathway [18] may be such a normalization mechanism. Failure to normalize the increased gain and variance may lead to not only tinnitus and hyperacusis [20, 31, 32] but also excitation spread towards other brain areas controlling pain, fear or other emotional responses [61-63].

## Conclusion

There are two potential mechanisms allowing the central system to compensate for reduced peripheral input: Increasing central noise or increasing central gain. An inevitable consequence of both mechanisms is an increase in central variance, which can help explain both tinnitus and hyperacusis. An additive central noise, which compensates for elevated hearing thresholds like those seen in traditional hearing loss, is more likely to induce tinnitus than hyperacusis. In contrast, an increase in multiplicative central gain, which compensates for hidden hearing loss, is more likely to induce hyperacusis. The effects of compensatory mechanisms on central variance have been ignored in previous studies, but may account for the conflicting results in the generation and behavior of tinnitus and hyperacusis.

## Acknowledgements

The work was partially supported by the National Institutes of Health (5R01 DC015587). I thank Barbara Shinn-Cunningham, Paul Fuchs, Nick Lesica, Michelle Kaplowicz, Phillip Tran and Ye Yang for commenting on the manuscript.

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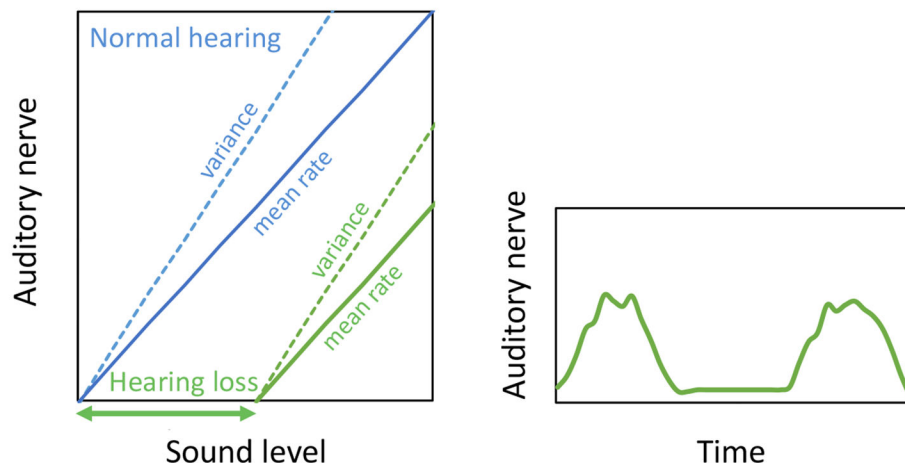
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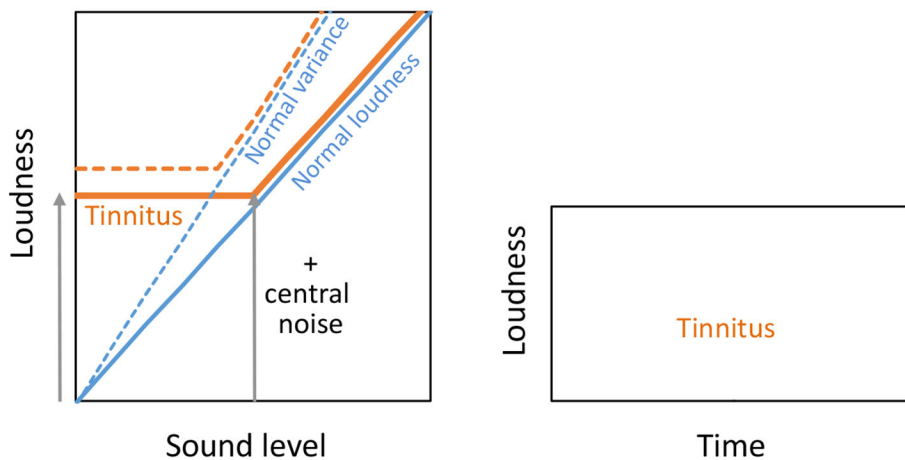
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**(a) Hearing loss reduces the overall auditory nerve activity**

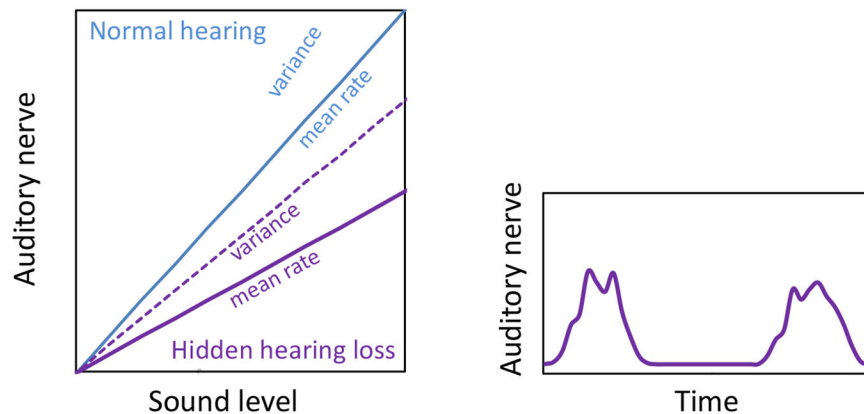
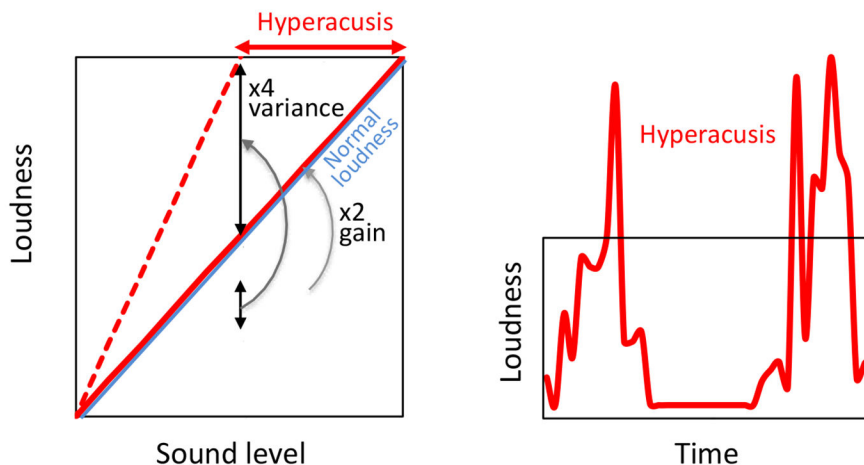


**(b) Additive central noise and variance induce tinnitus**



**Figure 1. Hearing loss, central noise and central variance.**

**(a)** Schematic effects of hearing loss on auditory nerve activity as a function of sound level (left panel) and time (right panel). Hearing loss elevates the threshold (double-  
 arrowed line below the x-axis). The normal activity is displayed as blue lines, whereas the activity with hearing loss is displayed as green lines. **(b)** Effects of adding central noise on loudness as a function of sound level (left panel) and time (right panel). The additive central noise (upward arrowed lines, left panel) restores normal loudness growth at high sound levels (solid sloping orange line=solid blue line, left panel) but increases loudness at the threshold or below (solid horizontal orange line, left panel). Both loudness mean and variance (dashed orange line, left panel) are the sum of their corresponding auditory nerve (green lines in Fig. 1(a)) and central noise values. The central noise generates tinnitus at or below the hearing threshold (labeled “Tinnitus” in both panels).

**(a) Hidden hearing loss reduces the auditory nerve activity slope****(b) Nonlinear central gain and variance induce hyperacusis****Figure 2. Hidden hearing loss, central gain and central variance.**

**(a)** Schematic effects of hidden hearing loss on auditory nerve activity as a function of sound level (left panel) and time (right panel). Similar to Figure 1(a), except for the purple lines which represent the hidden hearing loss. **(b)** Effects of central gain on loudness as a function of sound level (left panel) and time (right panel). The multiplicative central gain (a factor of two in this case; “x2 gain” as shown by the right curved arrow line, left panel) restores mean normal loudness growth at all sound levels (solid diagonal red line=solid blue line, left panel) but increases the amount of the central variance by a factor of four (“x4 variance” as shown by the left curved arrow line, left panel). The nonlinearly increased central variance generates hyperacusis at high sound levels (labeled “Hyperacusis” in both panels).