

# Clinical measures for investigating hidden hearing loss

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The present study compared clinical measures of auditory function in two listener groups prone to hidden hearing loss relative to a control group: a) listeners with tinnitus, and b) listeners with a history of noise-exposure. Auditory brainstem response (ABR) wave I, III and V were measured in response to a 4-kHz tone burst to quantify the level-growth of wave I and the amplitude difference between waves I-III and I-V. In addition, speech-in-noise performance using “Dantale I” and the Danish hearing in noise test (HINT) were assessed. The ABR wave-I level growth showed no difference between the tinnitus-, noise-exposed- and control group. The listeners with tinnitus had, however, significantly larger wave I-III differences indicating a gain at brainstem level. While the ABR results support that the wave I-III difference can be used as a physiological indicator of tinnitus, none of the applied audiological methods show signs of a noise-induced hidden hearing loss in the tested listener groups.

## INTRODUCTION

It has been a common assumption that temporary threshold shifts (TTS) following a noise-exposure were not hazardous as the observed pathology and shift in threshold were, as the name suggests, temporary. It was further assumed that hazardous sound levels, causing permanent deficits, primarily targets and damages outer hair cells (OHC) (Puel *et al.*, 1988; Lawner *et al.*, 1997). Such damage causes reduced sensitivity to soft sounds which can be assessed with standard pure-tone audiometry. Recent animal studies suggest, however, that 40 dB TTS cause immediate permanent damage of the inner hair cell (IHC) synaptic ribbons and afferent type I nerve fibres prior to any involvement of the OHCs (Kujawa and Liberman, 2009). This damage was reflected in the ABR as significantly reduced amplitude of wave I in response to supra-threshold level stimuli, while thresholds measured using ABR wave V normalised. Following this acute synaptic damage, a slowly progressive loss of cell bodies in the spiral ganglion was observed (Kujawa and Liberman, 2009). This suggests that noise-exposure causing TTS can cause immediate synaptic damage and progressive nerve damage (i.e., noise-induced neural degeneration, NIND) without affecting threshold sensitivity to pure-tones. One explanation for the restoration of

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thresholds could be the finding that high spontaneous rate fibres (HSRFs) were largely unaffected by noise exposure, whereas the synaptic damage predominantly affected low spontaneous rate fibres (LSRFs) (Furman *et al.*, 2013). LSRFs have higher thresholds and have been suggested to be responsible for the coding of mid- to high-intensity stimuli (Lieberman, 1978; Taberner and Liberman, 2005). In addition to coding supra-threshold stimuli, it has also been suggested that LSRFs are critical for processing of auditory stimuli in the presence of high-level background noise (Costalupes *et al.*, 1984). The consequences of NIND are therefore assumed to not be reflected in the audiogram, and have been given the term “hidden hearing loss” (Schaette and McAlpine, 2011). Thus, if acoustic overexposure also causes NIND of the LSRFs in humans, this may help to explain auditory disorders defined as difficulties processing speech in challenging listening environments, despite normal pure-tone thresholds (Zhao and Stephens, 1996). NIND has also been suggested to be a potential contributor to tinnitus in the absence hearing loss (Schaette and McAlpine, 2011).

So far physiological evidence of NIND has been shown for both mice (Kujawa and Liberman, 2009) and guinea pigs (Furman *et al.*, 2013). In humans, it is not possible to expose listeners to noise in order to investigate its consequences on physiology and auditory perception. Therefore, efforts have been made to investigate deficits in listener groups with a history of noise-exposure using behavioural and physiological measures. The reported results are, however, inconclusive. Significantly lower ABR wave I amplitudes in response to high-level stimuli have been found in listener groups with a self-reported higher exposure history compared to a control group with less reported exposure history (Bramhall *et al.*, 2016; Liberman *et al.*, 2016). Liberman *et al.* (2016) also reported significantly poorer performance on speech recognition in noise in the high-exposure group compared to the control group. In addition, a relationship between ABR wave I amplitude and self-reported noise exposure for female listeners, but not male listeners, has been reported (Stamper and Johnson, 2015). The findings of these studies support the assumption that NIND also exists in human listeners. A large study performed with 129 normal-hearing listeners found, however, no correlation between ABR wave I amplitude and history of noise-exposure, or any correlation between behavioural performance and noise-exposure (Prendergast *et al.*, 2016). Hence, it has still to be revealed if NIND occurs in human listeners, and if NIND can explain auditory deficits such as tinnitus or impaired speech recognition in noise, in the presence of normal threshold sensitivity.

The present study investigates if listeners prone to hidden hearing loss will: a) show a shallower slope in the level-growth of wave I, b) have larger amplitude gap between waves I-III and I-V, c) show poorer speech-performance in noise than the control group, and d) if level-growth is correlated with speech-in-noise performance.

## METHOD

*Listeners:* Two test groups and a corresponding control group were included in the study: a) listeners with tinnitus who reported chronic tinnitus for a minimum of one year (tinnitus group;  $n = 7$ , mean age  $26.8 \pm 1.9$  years), and b) listeners with a self-

reported history of over-exposure working in loud sound environments (professional musicians) for at least 5 hours a day, 5 days a week for at least 1 year (exposure group;  $n = 9$ , mean age  $25.6 \pm 4.1$  years). A loud sound environment was defined as an environment in which one would need to raise his or her voice in order to communicate. All listeners across the groups were young normal hearing (pure-tone thresholds  $\leq 15$  dB HL between 0.25 – 8 kHz) listeners between the ages of 18-35 years. The control group consisted of 9 listeners (mean age = 25.11 years  $\pm 4.7$ ). All participants provided informed consent and all experiments were approved by the Science-Ethics Committee for the Capital Region of Denmark (reference H-16036391).

*ABR*: ABRs were recorded using the Interacoustics Eclipse ABR system (EP15/EP25). Disposable non-invasive inverting electrodes were attached to the mastoids, a non-inverting electrode was placed on the middle of the forehead just below the hairline, and the ground electrode was placed below the non-inverting electrode. An impedance of  $< 3$  k $\Omega$  was ensured before initiating the measurement. Listeners were instructed to relax and preferably sleep while lying in an electrically shielded sound proof booth. 4-kHz tone burst stimuli of 1.25 ms, using Blackman window, were presented monaurally using ER2 insert earphones at peak-equivalent sound pressure levels (peSPL) of 97, 102 and 107 dB peSPL. The stimuli were presented with alternating polarity at a rate of 11.1/s and the ABR waveforms were recorded from  $-5$  to 11 ms. Each measurement continued until a residual noise level of  $\leq 30$  nV was obtained or a maximum of 4000 sweeps were recorded. ABR wave I-V peak-to-trough amplitudes were selected manually.

*Discrimination score (DS)*: DS was measured using the “Dantale I” material comprising wordlists consisting of 25 single monosyllabic words in speech-shaped noise (Elberling *et al.*, 1989). For each ear 3 lists were presented at 3 different SNR levels (10, 5 and 0 dB SNR). The speech level was kept at a constant level of 70 dB, while the noise was started at 60 dB and increased in steps of 5 dB for each list. Scoring was kept in percentage correctly repeated words of the 25 presented words.

*Hearing in noise test (HINT)*: The Danish HINT sentences (Nielsen and Dau, 2009) were presented monaurally in speech shaped background noise of 70 dB SPL. The stimuli were generated in MATLAB (The Mathworks, MA, USA) and presented over headphones (Sennheiser HDA200). Lists of 20 sentences were presented, and the listener was asked to repeat the sentences after best ability. The speech level was adaptively adjusted dependent on the response of the listener. The test was always started with an SNR of 0, with an initial speech level of 70 dB SPL. Before each test, a list of 20 training sentences was completed to familiarize the listener with the test and to eliminate training effects.

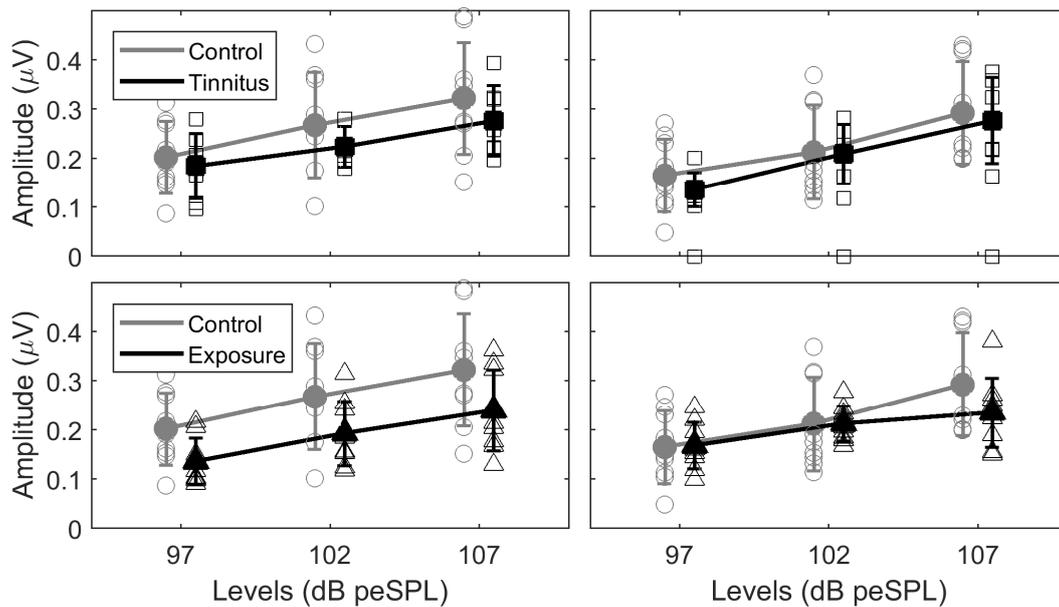
Speech recognition in noise was measured for the control and exposure group. However, not all listeners completed the speech task. For DS all the exposure group listeners, but only 5 out of 9 control listeners completed the task ( $n = 14$ ). For HINT

data was measured from 8 of the listeners in the exposure group, but only 2 in the control group ( $n = 10$ ).

*Statistical evaluation:* Statistics were calculated using Mann-Whitney U, and linear regression was calculated using the statistical software R (R Core Team, Vienna, Austria).

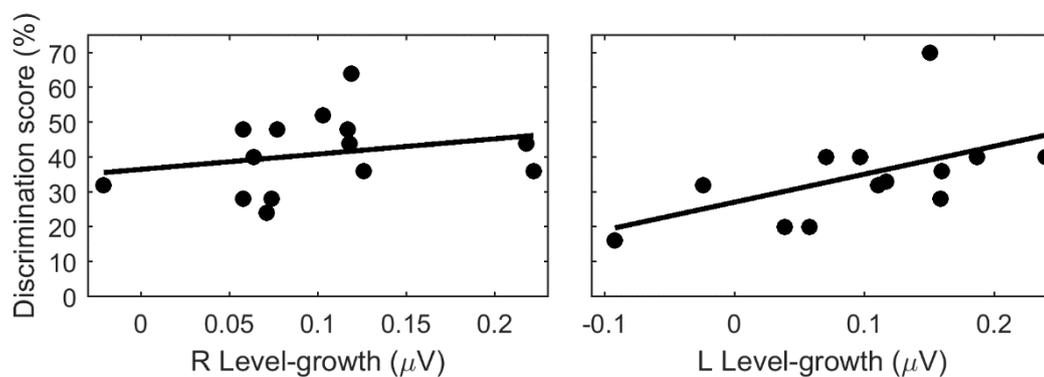
## RESULTS

Figure 1 depicts level-growth (amplitude of ABR wave I as a function of level increase) for the groups for right (left panel) and left (right panel) ear separately. The average level-growth from 97 to 107 dB peSPL for the right ear was  $0.108 \mu\text{V}$  for the control group,  $0.104 \mu\text{V}$  for the exposure group and  $0.092$  for the tinnitus group. Statistical analysis showed no significant differences of level-growth across listener groups. Significantly lower level-growth was, however observed for the left ear of the exposure group between 102-107 dB peSPL ( $U = 12$ ,  $p < 0.01$ , one-tailed) compared to the control group. The tinnitus group had significantly steeper level-growth from 97-102 dB peSPL ( $U = 17$ ,  $p < 0.05$ , two-tailed) compared to the control group.



**Fig. 1:** Wave I amplitude measured at 97, 102 and 107 dB peSPL. Results from the right ear are shown in the left panel and results from left ear are shown in the right panel. The upper panels show results from the control (grey circles) and tinnitus group (black squares). The bottom panels depict the exposure (black triangles) and the control group (grey circles). Mean values across groups are shown as solid markers and the individual data are shown as open markers.

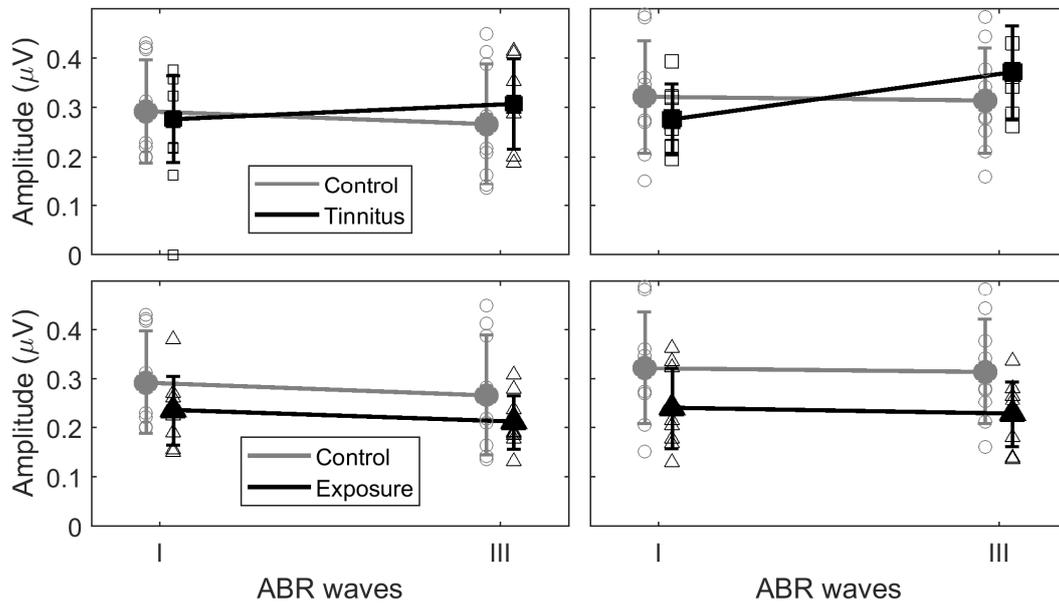
Figure 2 shows the results of the discrimination score (DS) as a function of the level growth. No significant difference was observed between the DS of the two groups for the right ear values ( $U = 33, p > 0.05$ ), but a significant difference was observed for the left ear ( $U = 20.5, p < 0.05$ , one-tailed). The Pearson correlation coefficient also showed a significant positive correlation between level-growth and DS with 0 dB SNR (the most challenging SNR) on the left ear ( $r = 0.53, p < 0.025$ , one-tailed). However, there was no correlation between these two variables for the right ear ( $r = 0.25, p > 0.05$ ). Measures of the Danish HINT did not show significant differences across groups, and no significant correlations between HINT and level-growth were found on either right ( $r = 0.25, p < 0.05$ , one-tailed) or left ( $r = 0.15, p < 0.05$ , one-tailed) ear of the listeners.



**Fig. 2:** DS measured with an SNR of 0 dB SNR as a function of ABR wave I level-growth for right ear (left graph) and left ear (right graph).

Figure 3 shows the difference in amplitude between ABR waves I-III between the control and tinnitus group (two upper panels) and the control and exposure group (bottom two panels) measured at a level of 107 dB peSPL. Significantly larger amplitude difference between waves I-III was observed for the listener group with tinnitus compared to the control group for both right ( $U = 15, p < 0.025$ , one-tailed) and left ear ( $U = 12, p < 0.01$ , one-tailed). This significant difference was not observed between the control and exposure group either for the right ( $U = 35, p > 0.05$ ) or left ear ( $U = 32.5, p > 0.05$ ).

No significant difference between ABR waves I-V was observed between the exposure and control group for right ( $U = 33, p > 0.05$ ) or left ear ( $U = 37, p > 0.05$ ) nor for the tinnitus and control group right ( $U = 28.5, p > 0.05$ ) or left ear ( $U = 22, p > 0.05$ , one-tailed).



**Fig. 3:** Amplitude difference between ABR waves I-III for right (left panels) and left ear (right panels). The upper graphs show results from the control (grey circles) and tinnitus group (black squares), while the bottom graphs depict the exposure (black triangles) and the control group (grey circles). Mean values across groups are shown as solid markers and the individual data are shown as open markers.

## DISCUSSION

The hypothesis of the current study was that if NIND occurs in human listeners (Kujawa and Liberman, 2009), ABR wave I level-growth will be significantly lower for a group with a history of working in higher-level sound-exposure or with chronic tinnitus with a normal audiogram. This hypothesis was not supported by the data.

Significantly lower level-growth was only found for the exposure group on the left ear between 97 and 102 dB peSPL ( $U = 12$ ,  $p < 0.01$ , one-tailed). Despite of this a significant correlation ( $r = 0.53$ ,  $p < 0.025$ , one-tailed) between level-growth and DS was observed for the left ear of listeners in the control and exposure group. Left ear DS was in fact also significantly poorer in the exposure group compared to the control group ( $U = 20.5$ ,  $p < 0.05$ , one-tailed). These data and the fact that DS was not correlated with age ( $r = 0.03$ ,  $p > 0.05$ ) could thus support a potential relationship between the pathology of noise-induced synaptic and neural degeneration and auditory disorders despite normal audiogram. However, level-growth was also significantly correlated with age for both right ( $r = 0.45$ ,  $p < 0.05$ , one-tailed) and left ear ( $r = 0.49$ ,  $p < 0.025$ , one-tailed). Multiple regression was performed to take the age variable into account. This reinforced the significant

correlation between DS and level-growth ( $r = 0.61$ ,  $p < 0.025$ , one-tailed). For the right ear this relationship can be rejected as level-growth and DS did not correlate significantly ( $r = 0.25$ ,  $p > 0.05$ ). The lack of significant difference on the HINT scores of the groups and correlation with level-growth suggests that NIND does not occur in humans. However, since the HINT material consists of natural sentences, it cannot be ruled out that cognitive abilities could have affected the results.

The hypothesis that the two groups assumed prone to NIND show larger amplitude differences between waves I-III was not confirmed for the exposure group relative to the control group. A significant difference between the tinnitus and control group was however confirmed with significantly larger amplitude difference between waves I-III for both right ( $U = 15$ ,  $p < 0.025$ , one-tailed) and left ear ( $U = 12$ ,  $p < 0.01$ , one-tailed) for the tinnitus group compared to the control group. This is in agreement with previous literature suggesting a relationship between the diagnosis of tinnitus, despite normal threshold sensitivity, and neural gain at brainstem level (Hickox and Liberman, 2014; Knipper *et al.*, 2013; Schaette and McAlpine, 2011).

Despite the possibility that NIND is absent in the tested listeners, one might speculate that the results of the present study can be explained by individual susceptibility to noise and developing hearing impairment or NIND. In such a case, the grouping variable ‘noise exposure’ might reduce the significance of the results.

## CONCLUSION

The current study did not find evidence of reduced ABR wave I level-growth in groups assumed prone to NIND using clinical measures. The findings of this study cannot confirm the presence of NIND in human listeners. The significant correlation between level-growth and DS on the left ear, however support the assumption that poorer speech recognition in noise, despite normal audiometric thresholds, can be attributed to loss of LSRFs. Furthermore, the findings of increased amplitude difference between waves I-III in the listeners with tinnitus support evidence of a relation between hyperactivity in the brainstem and tinnitus. Overall, the results of the clinical measures used in the current study either suggest that NIND is not present in the tested listeners or that these measures are not sensitive enough to reveal a clear connection between noise exposure and NIND in human listeners.

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