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Research Paper

Evaluation of dichotic listening performance in normal-hearing, noise-exposed young females

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A B S T R A C T

Recent animal studies have shown that intense noise exposures that produce robust temporary threshold shift (TTS) can inflict irreversible damage to the synaptic connections between the inner hair cells and auditory neurons. It was hypothesized that noise-induced cochlear synaptopathy may cause impaired acoustic encoding in the central auditory nervous system leading to impaired speech perception, particularly in challenging listening situations. The aim of the study was to evaluate the influence of high noise exposure background (NEB) on dichotic listening performance, speech-in-noise performance, and auditory brainstem responses (ABR) measured in young females with normal audiograms. The central hypothesis was that individuals with high NEB would exhibit reduced ABR wave I amplitude and subsequently would exhibit poorer performance on speech-in-noise and dichotic listening. In a sample of 32 females (14 with high NEB and 18 with low NEB) aged 18–35 years, the study compared behavioral hearing thresholds (from 250 to 16000 Hz), distortion-product otoacoustic emissions (DPAOEs, 1000–16000 Hz), click-evoked ABR, QuickSIN signal-to-noise ratio (SNR) loss and dichotic digit test (DDT). The results showed no clear association between NEB, and hearing thresholds, DPOAEs, click-evoked ABR measures, and QuickSIN SNR loss. Individuals with high NEB revealed significantly lower DDT scores and evidence of reduced right ear advantage compared to individuals with low NEB. The poorer performance in DDT and the ear asymmetry in DDT scores with normal ABR findings suggest that high NEB might alter the hemispheric organization of speech-sound processing and cognitive control. The clinical significance of the present findings is discussed.

1. Introduction

Intense noise exposures that produce robust temporary threshold shifts (TTS) can inflict irreversible damage to the synaptic connections between the inner hair cells (IHCs) of the cochlea and auditory nerve fibers in animals (Kujawa and Liberman, 2009; Lin et al., 2011; Furman et al., 2013; Liberman and Liberman, 2015; Kujawa & Liberman, 2015; Lobarinas et al., 2017). This noise-induced cochlear synaptopathy cannot be detected by evaluating hearing thresholds because noise exposures do not always cause loss of IHCs or outer hair cells (OHCs). However, it has been suggested that noise-induced synaptopathy would manifest as auditory processing difficulties in noise in the absence of clinically elevated behavioral hearing thresholds (Liberman & Liberman, 2015; Bharadwaj et al., 2014; Plack et al., 2014). It is not yet clear to what extent animal findings of noise-induced cochlear synaptopathy translate to humans, and what the exact nature of any of its supra-threshold perceptual consequences is. This topic is subject to intense scientific investigation.

It is well documented that youth are exposed to potentially hazardous levels of recreational noise, which may lead to noise-induced hearing loss (Carter et al., 2014). Recent reports suggest that almost 90% of youth (~15–25 years) report that they listen to music on a regular basis, with 26% listening to music for more than 3 h per day, and 48% reporting that their typical listening level is at a high or near-to-maximum volume (Vogel et al., 2009; Vogel et al., 2012). Additionally, personal music players have been shown to exceed damaging sound pressure levels at high volume control settings (Breinbauer et al., 2012). Research on the auditory lifestyle of college students has shown that almost 50% were exposed to potentially harmful music, 44% used noisy equipment without hearing protection, and almost 29% of them worked in a noisy

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environment (Rawool and Colligon-Wayne, 2008) suggesting that this population might be susceptible to cochlear synaptopathy, noise-induced hearing loss, and tinnitus.

Several studies have reported that individuals with high noise exposure may experience supra-threshold hearing difficulties including poorer speech understanding in noisy backgrounds (Stephens, 2003; Hope et al., 2013; Suting, 2016; Pienkowski, 2017), altered speech-sound discrimination (Brattico et al., 2005), impaired attentional control (Kujala et al., 2004; Bressler et al., 2017), and temporal processing difficulties (Stone et al., 2008). These studies observed an inverse relationship between noise exposure and supra-threshold speech perception measures. However, the underlying pathophysiological mechanisms for supra-threshold hearing difficulties in a challenging environment remained poorly understood. It was hypothesized that cochlear synaptopathy may reduce encoding precision of supra-threshold sound in the auditory subcortical pathways which may manifest as a speech perception deficit with normal audiograms (*e.g.*, Valderrama et al., 2018; Paul et al., 2018; Bramhall et al., 2017; Le Prell and Clavier, 2017; Prendergast et al., 2017; Fulbright et al., 2017; Grinn et al., 2017; Guest et al., 2017; Yeend et al., 2017; Liberman et al., 2016; Stamper and Johnson, 2015a,b; Bharadwaj et al., 2014).

The first direct investigation of cochlear synaptopathy in humans was published by Stamper and Johnson (2015a,b), who found that the amplitude of wave I of the ABR in response to high-intensity clicks was negatively correlated with noise exposure background (NEB). NEB was evaluated using a questionnaire, which quantified the amount of high-intensity sound encountered over the last 12 months. The authors observed that their high NEB group contained a majority of male participants that might be a potential confound for showing weaker ABRs than females due to sex-related confounding factors. Their re-analysis found a significant decrease in ABR wave I amplitudes as a function of NEB for females, but no such relation was observed for males (Stamper and Johnson, 2015b). Liberman et al. (2016) found that individuals with high NEB had elevated behavioral hearing thresholds at ultra-high frequencies, an elevated summating potential to action potential ratio, poor performance on word recognition in noise and heightened reaction to sounds. Similarly, Bramhall et al. (2017) found evidence of reduced ABR wave I amplitudes in young military veterans with normal audiograms. Grose et al. (2017) reported evidence of reduced ABR wave I amplitudes in individuals with a history of frequent attendance to loud music events but with no abnormality in psychophysical or speech perception deficits. Most of the recent studies testing young adults ($\leq$35 years) found no evidence of a reduction in ABR wave I amplitude or subsequent supra-threshold deficits in speech-in-noise tasks (Prendergast et al., 2017; Fulbright et al., 2017; Grinn et al., 2017; Guest et al., 2017; Yeend et al., 2017; Valderrama et al., 2018).

(Central) auditory processing (CAP) tests, which are sensitized to identify a deficit in the central nervous system (Musiek et al., 2018) might be useful to delineate the effects of high NEB on the central auditory system. Dichotic speech listening performance has been widely used to measure CAP performance in children and adults. In dichotic listening tasks, two different auditory stimuli are presented simultaneously to the right and left ears and the listener is required to report what was heard in both ears (i.e. "free recall" condition) or in one ear ("directed recall" condition). Dichotic tests challenge the auditory system and cognitive functioning with tasks like attention focusing and use of working memory (Fischer et al., 2017). The Dichotic Digit Test (DDT), in which single-syllable numbers are presented simultaneously in each ear, usually in single, double or triple-digit pairs, is widely used to evaluate CAP for diagnosis of (central) auditory processing disorder ((C)APD) (e.g., Musiek et al., 2018; Musiek et al., 1991; Gates et al., 2008; Gates et al., 2010; Gates et al., 2011). The DDT has a short administration time, good test-retest reliability, simple scoring process and age-matched norms that make it suitable to use in clinics (Strouse and Wilson, 1999; Strouse and Hall, 1995). The dichotic test performance demonstrates an inverse relationship with age, cognitive decline and cognitive impairment (Jerger et al., 1995; Wilson and Jaffe, 1996; Strouse et al., 2000; Hällgren et al., 2001; Gates et al., 2002; Gates et al., 2011; Roup et al., 2006; Fischer et al., 2017). The dichotic listening skills were found to be a strong predictor of the speech-in-noise deficit in older adults with hearing impairment (Lavie et al., 2013). Dichotic listening and speech-in-noise perception require listening to competing signals and they both decline with age, which suggests that the underlying neurophysiological mechanism for both skills might be overlapping (Martin and Jerger, 2005). However, the effects of high NEB on dichotic listening has not been investigated well in the literature.

The objective of the present study was: (1) to evaluate the influence of high NEB on ABR measures (amplitude and latency of wave I, III, and V), and (2) to evaluate the influence of high NEB on speech-in-noise (as measured by QuickSIN) and dichotic listening performance (as measured by DDT). It was hypothesized that individuals with high NEB would exhibit reduced ABR wave I amplitude and subsequently would exhibit poorer performance on QuickSIN and DDT. A recent study showed that analysis of males and females together might lead to erroneous results even if the statistical analysis is performed to account for sex difference (Milon et al., 2018). Therefore, this study investigated the above-stated hypotheses in a sample of young females with normal audiograms to avoid sex bias.

2. Materials and methods

The Institutional Review Board of Northern Arizona University reviewed and approved the study protocol. Subjects were recruited from students enrolled at the Flagstaff Mountain Campus of Northern Arizona University. A written informed consent was obtained for each subject prior to the data collection process.

2.1. Screening questionnaire

A recruitment flyer was distributed in three classes at the Flagstaff campus of Northern Arizona University. The students were instructed to fill out the questionnaire (Supplementary File S1) and provide their contact information. This survey included an assessment of five major areas: demographic details, routine acoustic exposure, tinnitus, smoking, and quality of hearing. (1) Demographic details: Participants were asked about their age, gender and ethnicity. (2) Routine acoustic exposure: Acoustic exposure was estimated via a self-report questionnaire (Johnson et al., 2017). This survey has been validated to estimate overall acoustic exposure and has been utilized in previous research to quantify noise exposure in young adults (e.g., Bhatt, 2018; Stamper and Johnson, 2015a,b). It assessed nine specific known areas of high acoustic exposure. These included exposure to six areas of noise exposure: occupational noise, power tools, heavy equipment, commercial sporting or entertainment events, motorized vehicles, small aircraft; and three areas of music exposure: music instrument playing, music listening via personal earphones, and music listening via audio speakers. The survey included questions about frequency (i.e. how often) and duration (i.e. how long) of noise exposures. The responses were elicited using a forced choice method. Responses were rated categorically to calculate the overall noise dose that was reported as $L_{Aeq8760h}$. Here, "L" represents sound pressure level measured in dB, "A" presents use of an Aweighted frequency response, "eq" represents a 3-dB exchange rate for calculation of the time/level relationship, and "8760 h" represents the total duration of noise exposure in hours over one year (365 days/year X 24 h/day). Further details of the survey can be found elsewhere (Megerson, 2010; Johnson et al., 2017). (3) Tinnitus: The questions inquiring about tinnitus were adopted from the National Health and Nutrition Examination Survey (2012). This section inquired about tinnitus with an opening question: "In the past 12 months, have you been bothered by ringing, roaring, or buzzing in your ears or head that lasts for 5 min or more?". Tinnitus was classified into two categories: Present Bothersome Tinnitus and Absent Bothersome Tinnitus. (4) Smoking: This section inquired about smoking with an opening question: "Do you or have you smoked tobacco?" If the participant answered positively to this question, then the follow-up question was: "What types of smoking do you prefer, or have preferred, on a regular basis? (percentage values of all selected choices must add up to 100%)". Smoking was classified into two categories: present or absent smoking history. (5) Quality of hearing: The Speech, Spatial and Quality of Hearing Scale – 12-item version (SSQ12) was used to measure the self-reported quality of hearing. The SSQ12 provides similar results to SSQ49 (49-item version) in a large clinical research sample (Noble et al., 2013).

2.2. Subjects

An initial sample of 70 female respondents aged 18–35 years was obtained from three undergraduate classes. A cut-off score of 79 was used to identify 15 females with high NEB (see Johnson et al., 2017 for further details) and a cut-off score of 70 was used to identify 22 females with low NEB. These subjects were invited to participate in a laboratory session. An otoscopic exam was performed on all participants during the laboratory session. Those with normal otoscopic findings were tested with pure tone audiometry. All audiometric measures described in this study were collected in a sound-treated booth meeting ANSI standards (ANSI S3.1–1999). Audiometric thresholds were obtained using GSI-61 (Grason-Stadler, Eden Prairie, MN) at 250, 500, 1000, 2000, 3000, 4000, 6000 and 8000 Hz with ER-3A insert receivers (Etymotic Research. Inc, Elk Grove Village, IL) and at 9000, 10000, 11200, 12500, 14000 and 16000 Hz with HDA200 high-frequency receivers (Sennheiser Electronic Corporation, Wedemark, Germany) using the modified Hughson-Westlake procedure. Participants with hearing thresholds ≤15 dB HL at the audiometric frequencies from 250 to 8000 Hz were tested with tympanometry. Tympanometry was performed using a 226 Hz probe tone presented through Titan IMP440 (Interacoustics, Middelfart, Denmark). Participants with normal tympanograms (static compliance between 0.35 and 1.75 cc and peak pressure value between +50 and −100 daPa) in both ears were considered for further testing. Along with otoscopy and tympanometry, an informal interview was conducted to rule out active health conditions. Subjects reporting good health and no systemic diseases, neurological or immunological disorders were included in the study. Five subjects (one with high NEB and four with low NEB) who did not meet the above-listed criteria were excluded from further testing. The included participants, 14 with high NEB and 18 with low NEB, participated in the present study. Among participants with high NEB, 13 reported that they prefer the right hand and one reported an equal preference to both hands for routine activities. Among participants with low NEB, 14 reported that they prefer right hand, 3 reported left hand and one reported an equal preference to both hands for routine activities. The participants were non-musicians (i.e. no exposure to formal musical training for ≥5 years).

2.3. Clinical measure of speech-in-noise perception

The speech-in-noise performance was assessed with the QuickSIN because it is a widely used clinical test with superior ability to separate performance between groups of participants with normal hearing and hearing impairment (Wilson et al., 2007). Six sentences were presented binaurally at 70 dB HL fixed speech level in a background of four-talker babble noise (three females and one male) through insert earphones (ER-3A; Etymotic Research). The first set of six sentences was presented at +25 dB signal-to-noise ratio (SNR), with the SNR decreasing by 5 dB for each subsequent sentence down to 0 dB SNR. Five keywords in each sentence were marked as correct or incorrect. The total number of keywords repeated correctly in each set of six sentences was subtracted from 25.5 to obtain the SNR loss in dB, defined as the difference between the individual's SIN threshold and the average SIN threshold (Killion et al., 2004). The SNR loss scores were averaged over the three lists to obtain the final SNR loss. A lower SNR loss score indicated better speech-in-noise performance. QuickSIN performance has previously shown reliable association with the brainstem measures making it suitable to investigate deficit in the auditory brainstem nuclei (Anderson et al., 2013).

2.4. Distortion product otoacoustic emissions (DPOAEs) measurement

DPOAEs were measured using the SmartDPOAE system (version 5.10, Intelligent Hearing System, Miami, FL) connected to an ER-10D probe (Etymotic Research. Inc, Elk Grove Village, IL). DPOAEs at 2F1–F2 were measured for F2 values ranging from 1000 to 16000 Hz in two data points/octave. A stimulus frequency ratio of 1.22 and stimulus–level combinations of 55/40, 65/55, and 75/75 dB sound pressure level (SPL) were used (Poling et al., 2014). A maximum of 64 sweeps was presented until one of the stopping conditions was reached: SNR>12 dB or a noise floor of <20 dB SPL. DPOAE strength was calculated by averaging the DP responses for F2 at 3130, 4422 and 5244 Hz in both ears. DPOAE strength was used as a covariate in the statistical analysis to control for the effect of OHC function on ABR wave I amplitude while investigating the relationship between NEB and ABR wave I amplitude (see Bramhall et al., 2017 for further details).

2.5. Auditory brainstem responses (ABR) measurement

Testing was conducted using the Intelligent Hearing System (IHS) SmartEP system (Intelligent Hearing System, Miami, FL). Participants were instructed to relax while reclined on a table within a sound-treated booth meeting ANSI standards (ANSI S3.1–1999). Standard 10 mm gold cup EEG disk electrodes were attached to the following locations using Ten20 conductive paste, Fpz (ground), high forehead (non-inverting), and A1 and A2 (inverting for the left and right ears, respectively). These areas were prepped using an alcohol wipe and a Nuprep skin prep gel for effectively reducing the inter-electrode impedance values. Impedance values at each electrode site were monitored to remain less than 3000 Ohms with an inter-impedance value less than 2000 Ohms. These impedance values were monitored throughout the testing procedure.

A click stimulus, 100 μs in duration, was delivered via electrically shielded ER-3A insert receivers. Clicks were monaurally presented at 80 dB nHL (85.7 ± 0.3 dB SPL, calibration in an IEC-711 ear simulator) with alternating polarity at two stimulus rates: 11.1/sec and 71.1/sec. The electrodes were connected to a dual channel preamplifier. The preamplifier was connected to the USB box with a fiber optic cable. Recording parameters included a gain of 100,000 and band-pass filtering from 1 Hz to 5000 Hz. ABRs were collected with a sampling frequency of 40000 Hz, a pre-stimulus window of −12.8 to 0 ms and a post-stimulus window of 0–12.8 ms. The ABR waveforms were measured using 2048 sweeps (1024 sweeps per click polarity) and the average waveform was used for the statistical analysis.

Two independent judges separately identified peak to trough amplitudes of waves I, III and V using visual overlay cursors on a computer screen. The first judge collected the waveforms during the laboratory session but was not provided with the subject information. The second judge was blinded to subject information during ABR waveform analyses. Any inter-scorer disagreements between the two judges were resolved by reviewing the data together. A composite measure of the ABR wave I amplitude was calculated. In order to create this measure, Z scores of ABR wave I amplitude in four conditions (right ear with 11.1/sec and 71.1/sec stimulus rate, and left ear with 11.1/sec and 71.1/sec stimulus rate) were calculated. The composite was an average of the four constituent Z scores.

2.6. Dichotic digits test

The free recall DDT was administered with 25 sets of triple-digit pairs (3 digits presented to each ear simultaneously), with single-syllable numbers 1 through 10 (excluding 7). The free recall tasks required the participants to repeat all the six digits presented in both ears in a pair (see Strouse and Wilson, 1999 for further details). The presentation level was set at 70 dB HL. DDT was administered with a calibrated GSI-61 audiometer (Grason-Stadler, Eden Prairie, MN) with ER-3A receivers. For training and practice, three examples of triple-digit pairs were presented prior to testing. The sum of the right and left ear scores was used as the measure of function on the free recall DDT. Therefore, the possible range of the correct number of repeated digits was 0–150 (75 digits per ear). The correct number was converted to the percent correct scores for right ear (DDT_R), left ear (DDT_L), and both ears ($DDT_{C\ (combined)} = (DDT_R + DDT_L)/2$). Further details of the test can be found elsewhere (Fischer et al., 2017). The advantage (or laterality) index (Marshall et al., 1975; Hugdahl, 2004; Rimol et al., 2006; Iliadou et al., 2010) used to evaluate the ear advantage of the participants tested in the present study is the following: Advantage index = [(correct right ear score − correct left ear score)/(correct right ear results + correct left ear results)]*100. The index varies between −100 and +100. The positive values indicate right ear advantage, negative values indicate left ear advantage and zero indicates absent ear advantage.

2.7. Statistical analysis

All statistical analyses were performed using the IBM SPSS version 25 statistics package. The repeated measure ANOVA model was utilized to identify the main effect of NEB on hearing thresholds, DPOAEs and ABR measures. The main effect of NEB on audiometric thresholds was evaluated using a repeated measure ANOVA model where the within-subject factors were hearing thresholds at each audiometric frequency from 250 to 16000 Hz (14 levels), and the between-subject factor was NEB. The main effect of NEB on DPOAEs was evaluated using a repeated measure ANOVA model where the within-subject factors were DPOAE amplitude at each F2 frequency from 1000 to 16000 Hz (9 levels), and the between-subject factor was NEB. The repeated measure ANOVA models were created for each primary tone combination. The main effect of NEB on ABR amplitude measures was evaluated using a repeated measure ANOVA model using three within-subject factors: ABR amplitude (wave I, III and V), stimulus rate (11.1/sec and 71.1/sec), and ear (right and left) and one between-subject factor: NEB. A similar analysis was performed to evaluate the effects of NEB on ABR latency measures.

The ABR wave I data were nested at three levels to investigate the effect of NEB on ABR measures. The amplitude data were nested within ear (two levels: right and left) and ear was nested in rate (two levels: 11.1/sec and 71.1/sec). The mixed model repeated measure ANOVA was performed to analyze the effects of NEB on wave I amplitude while controlling the effects of DPOAE strength, rate and ear. Similar analyses were performed to investigate the effects of NEB on ABR wave III and V amplitude and latency measures. We also used a multiple linear regression model with a dependent variable, composite of wave I amplitude, and four predictors: NEB, tinnitus, QuickSIN SNR loss, and DPOAE strength. This model allowed accounting for tinnitus, QuickSIN SNR loss, and DPOAE strength while investigating the relation between NEB and composite of wave I amplitude. A multiple linear regression model with a dependent variable, DDT_C, and four predictors: NEB, tinnitus, SSQ12, and a composite of wave I amplitude was utilized to evaluate the effects of the predictors on DDT_C. A similar analysis was performed for dependent variables: QuickSIN and advantage index. The predictors were added to the models using the Enter method and then removed from the model using a backward Stepwise method if they did not significantly contribute to the prediction of the variance in the dependent measures ($p < 0.1$).

3. Results

3.1. Demographic details

Among the study sample of 32 female participants, 26 (81.2%) reported predominant European American ethnicity and six (18.8%) reported other (including multiracial) ethnic background. Two participants reported that they smoked tobacco at least once in their lifetime. Almost 22% (7 participants: 5 with high NEB and 2 with low NEB) reported that they perceived bothersome tinnitus that lasted for at least 5 min in the past year.

3.2. Comparison of hearing thresholds between participants with high and low NEB

The repeated measure ANOVA revealed that hearing thresholds from 250 to 16000 Hz were not significantly different between participants with high and low NEB in the right ear ($F(1,30) = 1.069$, $p = 0.30$) and in the left ear ($F(1,30) = 0.410$, $p = 0.527$). Fig. 1 presents average hearing thresholds as a function of audiometric frequency between participants with high and low NEB. The results showed that audiometric thresholds were not significantly different between the experimental groups.

3.3. Comparison of speech-in-noise measures between participants with high and low NEB

An independent sample *t*-test revealed that QuickSIN SNR loss was not statistically significant between the participants with high and low NEB ($MD = -0.19$, $t(30) = -0.797$, $p = 0.43$). Similarly, there was no statistically significant difference for SSQ12 score between participants with high and low NEB ($MD = 0.174$, $t(30) = 0.389$, $p = 0.70$). QuickSIN SNR loss and SSQ12 showed no significant association ($r(30) = -0.104$, $p = 0.571$). A multiple regression analysis revealed no significant association between QuickSIN SNR loss, NEB, SSQ12, and tinnitus.

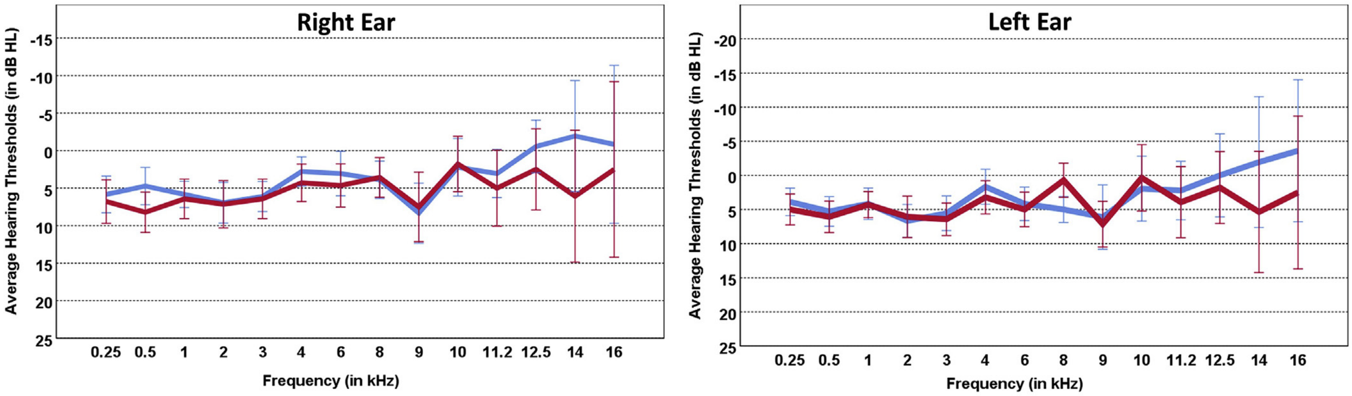

Fig. 1. Average behavioral hearing thresholds as a function of audiometric test frequencies between the high and low NEB groups. The blue and red lines represent hearing threshold data from the low and high NEB groups, respectively. The error bar indicates ±95% confidence interval. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

3.4. *Comparison of DPOAE amplitude between participants with high and low NEB*

The repeated measure ANOVAs were performed to determine the relation between DPOAEs and NEB at three stimulus levels, 55/40, 65/55, and 75/75 dB SPL. The results revealed no significant association between DPOAE amplitude measures and NEB at 55/40 (F(1, 30) = 2.052, $p = 0.16$), 65/55 (F(1, 30) = 1.145, $p = 0.29$) and 75/75 (F(1, 30) = 2.122, $p = 0.15$) primary tone combinations in the right ear. Similarly, the main effect of NEB was not significant at 55/40 (F(1, 30) = 0.76, $p = 0.78$), 65/55 (F(1, 30) = 0.855, $p = 0.36$), and 75/75 (F(1, 30) = 1.57, $p = 0.22$) primary tone combinations in the left ear. Fig. 2 presents average DPOAE amplitude as a function of F2 from 1000 to 16000 Hz for participants with high and low NEB.

3.5. *Comparison of ABR measures between participants with high and low NEB*

Supplementary file S2 presents the results of the mixed model repeated measure ANOVA. NEB revealed no significant relationship with wave I amplitude ($p = 0.77$). DPOAE strength was positively correlated to wave I amplitude ($p = 0.001$). We obtained no significant relationship between NEB and ABR wave III amplitude. Similarly, the main effect of NEB was not statistically significant for ABR wave I, III and V latency. NEB revealed a significant association with wave V amplitude indicating that subjects with high NEB exhibit higher wave V amplitude compared to subjects with low NEB ($p = 0.03$). However, the p value did not remain statistically significant after the Bonferroni correction was applied for the multiple comparisons (i.e. 0.05/6 = 0.008; threshold for statistical significance = 0.05; number of comparison/model = 6).

Similarly, the repeated measure ANOVA revealed that ABR wave I, III and V amplitude were not significantly different between participants with high and low NEB (F(1,30) = 0.223, $p = 0.64$). The main effect of stimulus rate was statistically significant (F(1,30) = 451, $p < 10^{-18}$). The main effect of ear was not statistically significant (F(1,30) = 2.44, $p = 0.12$). ABR wave I, III and V latency were not significantly different between participants with high and low NEB (F(1,30) = 0.413, $p = 0.52$). The main effect of stimulus rate was statistically significant (F(1,30) = 142, $p < 10^{-12}$), but the main effect of ear was not statistically significant (F(1,30) = 0.025, $p = 0.87$).

A multiple linear regression analysis with 4 predictors: NEB, tinnitus, QuickSIN SNR loss, and DPOAE strength, revealed that NEB

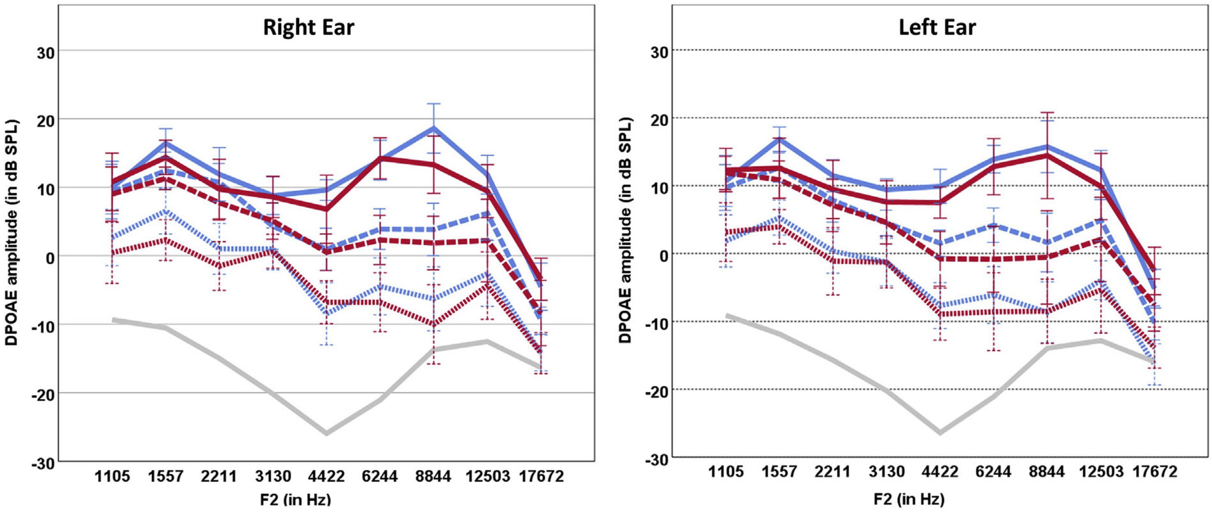

Fig. 2. Mean DPOAE levels as a function of F_2 frequency. The blue lines present DPOAE levels for individuals with low NEB and red lines present DPOAE levels for individuals with high NEB. The solid, long-dashed and dotted lines present the average DPOAE amplitudes obtained with the combinations of primary tones 75/75, 65/55, and 55/40, respectively. Error bars indicate ±95% confidence interval. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

showed no association with a composite of wave I amplitude ($\beta = -0.156$, $t(29) = -0.715$, $p = 0.481$). DPOAE strength revealed statistically significant relation with composite of wave I amplitude ($\beta = 0.076$, $t(30) = 2.852$, $p = 0.008$). No other predictors showed significant association with a composite of wave I amplitude. The results of the analyses revealed that ABR measures were not significantly different between participants with high and low NEB. Table 1 presents the average amplitude and standard deviation for amplitude and latency measures of ABR waves I, III and V. Fig. 3 presents grand average ABR waveforms between participants with high and low NEB.

3.6. Comparison of DDT measures between participants with high and low NEB

The regression analysis revealed that participants with high NEB showed significantly poorer DDT$_{\text{C}}$ score compared to participants with low NEB ($\beta = -8.394$, $t(28) = -3.531$, $p = 0.001$). Participants reporting bothersome tinnitus perception revealed significantly poorer DDT$_{\text{C}}$ score compared to participants without bothersome tinnitus perception ($\beta = -6.704$, $t(28) = -2.27$, $p = 0.031$). Participants reporting high SSQ12 scores revealed a significantly higher DDT$_{\text{C}}$ score ($\beta = 2.215$, $t(28) = 2.314$, $p = 0.028$). NEB, tinnitus and SSQ12 explained a significant proportion of variance in DDT$_{\text{C}}$ score with adjusted $R^2 = 0.329$, $F(3, 31) = 6.072$, $p = 0.003$. The Kolmogorov-Smirnov test revealed that the standardized residuals were distributed normally (Statistic = 0.137, $p = 0.134$). Composite ABR wave I amplitude showed no association with DDT$_{\text{C}}$ score ($\beta = -0.037$, $t(27) = -0.02$, $p = 0.98$). 3-pair DDT performance below the cutoff of the 99.7% CI for free recall condition was applied (Strouse and Wilson, 1999) to identify participants with clinically abnormal performance on the test. All of the participants with low NEB showed normal DDT scores in both ears. Among 14 participants with high NEB, 7 (50%) revealed abnormal DDT$_{\text{R}}$ and 4 (29%, all with abnormal DDT$_{\text{R}}$) revealed abnormal DDT$_{\text{L}}$ scores. The Chi-square statistics revealed that the observed differences in the frequency of normal versus abnormal DDT between the NEB groups were statistically significant for the right ear ($X^2(1, N = 32) = 11.52$, $p = 0.001$) and for the left ear ($X^2(1, N = 32) = 5.87$, $p = 0.015$).

Participants with high NEB revealed a significantly lower advantage index compared to participants with low NEB ($\beta = -2.177$, $t(30) = -2.262$, $p = 0.031$). Tinnitus ($\beta = -0.129$, $t(27) = -0.099$, $p = 0.92$), SSQ12 ($\beta = 0.186$, $t(27) = 0.415$, $p = 0.681$) and ABR wave I amplitude ($\beta = -0.888$, $t(27) = -1.084$, $p = 0.28$) showed no association with the advantage index. NEB explained a significant portion of variance in the advantage index with adjusted $R^2 = 0.117$, $F(1, 31) = 5.118$, $p = 0.031$. The Kolmogorov-Smirnov test revealed that the standardized residuals were distributed normally (Statistic = 0.13, $p = 0.184$). Fig. 4 presents DDT measures between the participants with high and low NEB.

3.7. Relationship between the composite of ABR wave I amplitude and speech perception measures

The composite of ABR wave I amplitude revealed no significant relationship with DDT$_{\text{R}}$ ($r(30) = 0.10$, $p = 0.57$), DDT$_{\text{L}}$ ($r(30) = 0.25$, $p = 0.16$), DDT$_{\text{C}}$ ($r(30) = 0.17$, $p = 0.34$) and QuickSIN SNR loss ($r(30) = -0.05$, $p = 0.74$) for the entire sample. The composite of ABR wave I amplitude revealed a statistically significant relationship with DDT$_{\text{L}}$ ($r(16) = 0.49$, $p = 0.03$) for a split sample with low NEB. No such relationship was observed for a split sample with high NEB. Similarly, no significant relationship was observed between the composite of ABR wave I amplitude, QuickSIN SNR loss, and SSQ12 scores. Fig. 5 presents scatter plots between the composite of ABR wave I amplitude and speech perception measures.

3.8. Relationship among SSQ12, DDT scores and QuickSIN SNR loss

QuickSIN SNR loss revealed a statistically significant relationship with DDT$_{\text{R}}$ ($r(30) = -0.376$, $p = 0.034$) and DDT$_{\text{C}}$ ($r(30) = -0.367$, $p = 0.039$). The correlation coefficient for QuickSIN SNR loss and DDT$_{\text{L}}$ did not achieve statistical significance ($r(30) = -0.322$, $p = 0.073$). The correlation coefficients for SSQ12 and DDT$_{\text{R}}$ ($r(30) = 0.252$, $p = 0.16$), DDT$_{\text{L}}$ ($r(30) = 0.316$, $p = 0.07$) and DDT$_{\text{C}}$ ($r(30) = 0.295$, $p = 0.10$) also failed to achieve statistical significance. Similarly, SSQ12 did not reveal a statistically significant relationship with DDT$_{\text{C}}$ ($r(30) = 0.17$, $p = 0.34$) or with QuickSIN SNR loss ($r(30) = -0.15$, $p = 0.39$). The SSQ12 score showed a statistically significant relation with DDT$_{\text{C}}$ ($r(16) = 0.61$, $p = 0.007$) when the analysis was run for a split sample with low NEB. No such relationship was observed for a split sample with high NEB. Fig. 6 presents the scatter plots for SSQ12, DDT scores and QuickSIN SNR loss.

4. Discussion

The present study examined the effects of high NEB on ABR, speech-in-noise and dichotic listening skills in a sample of young females with normal audiograms. It was hypothesized that the synaptic connections between cochlear IHCs and auditory neurons would be impaired due to high NEB leading to compromised auditory processing skills. Contrary to the hypothesis, the study found that: (1) individuals with high NEB did not reveal a statistically significant difference in behavioral hearing thresholds, DPOAEs, ABR measures and speech-in-noise performance, (2) individuals with high NEB, lower SSQ12 and tinnitus revealed lower DDT$_{\text{C}}$ scores, and (3) individuals with high NEB showed significantly lower values of advantage index compared to individuals with low NEB. These findings suggest that participants with high NEB have a dichotic listening deficit without revealing convincing evidence of a reduced ABR wave I amplitude.

Table 1
Average amplitude and latency of waves I, III and V for each stimulus rate, ear and NEB groups. The standard deviation values are listed in parentheses.

	Rate	NEB	Right ear			Left ear		
			Peak I	Peak III	Peak V	Peak I	Peak III	Peak V
			Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Amplitude	11.1/s	Low	0.41 (0.12)	0.37 (0.13)	0.65 (0.16)	0.43 (0.17)	0.33 (0.13)	0.60 (0.18)
		High	0.45 (0.14)	0.40 (0.19)	0.64 (0.20)	0.43 (0.10)	0.34 (0.15)	0.62 (0.18)
	71.1/s	Low	0.23 (0.06)	0.25 (0.08)	0.50 (0.14)	0.20 (0.09)	0.20 (0.07)	0.50 (0.16)
		High	0.17 (0.09)	0.25 (0.12)	0.54 (0.15)	0.16 (0.09)	0.20 (0.09)	0.60 (0.21)
Latency	11.1/s	Low	1.64 (0.09)	3.75 (0.16)	5.48 (0.18)	1.62 (0.14)	3.76 (0.19)	5.54 (0.20)
		High	1.61 (0.16)	3.77 (0.17)	5.57 (0.26)	1.62 (0.15)	3.76 (0.14)	5.57 (0.29)
	71.1/s	Low	1.83 (0.17)	4.03 (0.14)	5.94 (0.10)	1.76 (0.10)	4.02 (0.18)	5.93 (0.16)
		High	1.84 (0.21)	4.06 (0.20)	5.94 (0.20)	1.84 (0.17)	4.07 (0.22)	5.98 (0.27)

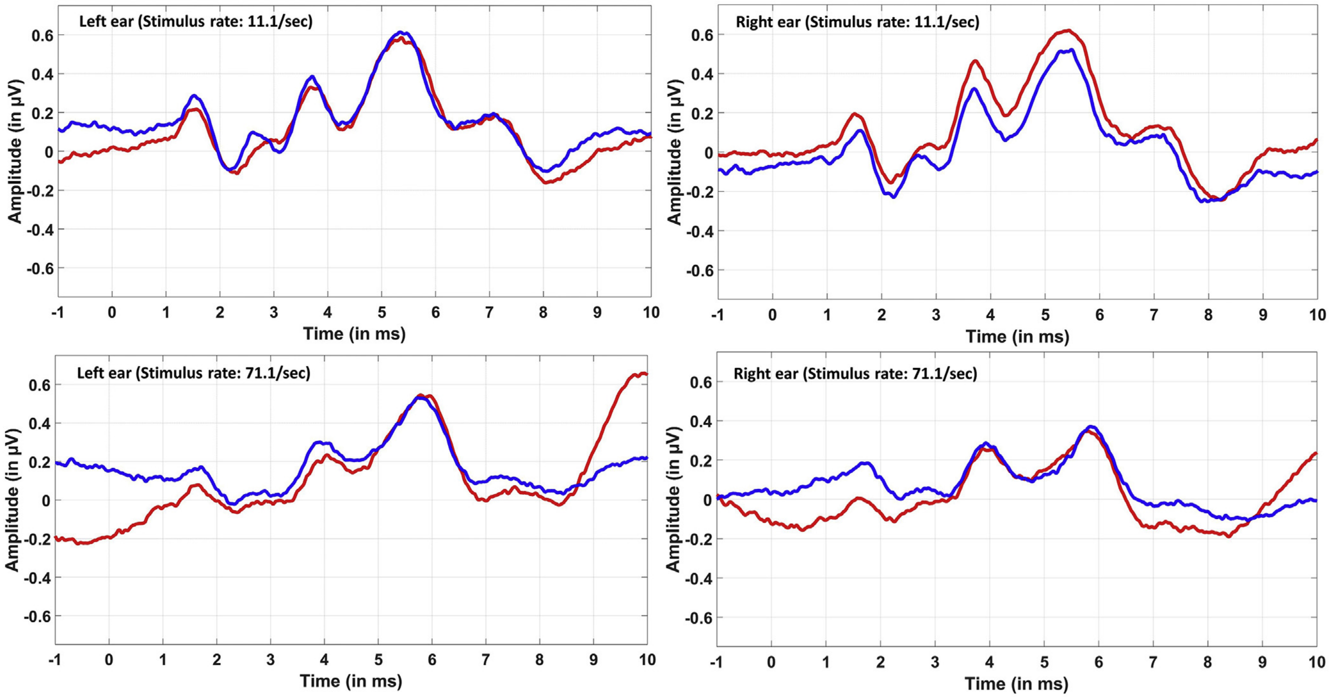

Fig. 3. Grand average ABR waveforms from individuals with high NEB (red line) and low NEB (blue line). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

The study obtained a significant correlation coefficient between DPOAE strength and ABR wave I amplitude. The results suggested that individuals with stronger DPOAE strength exhibited higher ABR wave I amplitude. DPOAE strength reflects the mechanical activity of the basilar membrane, with a higher strength value signifies a stronger cochlear amplifier (Dhar et al., 2009), and subsequently stronger input to the auditory afferent neurons. NEB revealed no association with DPOAE and ABR wave I amplitude. The association between NEB and wave V amplitude did not achieve statistical significance after the Bonferroni correction was applied for the multiple comparisons. Therefore, it was concluded that NEB was not correlated with DPOAE strength and ABR measures.

4.1. Noise-induced cochlear synaptopathy in animal and human research

The present study could not obtain a significant difference between ABR wave I amplitude between high and low NEB groups. This observation is consistent with some previous studies (Prendergast et al., 2017; Fulbright et al., 2017; Grinn et al., 2017; Guest et al., 2017; Yeend et al., 2017; Valderrama et al., 2018). There are several possible explanations for this finding. One possibility is that the noise exposure questionnaire (Johnson et al., 2017; Stamper and Johnson, 2015a) used by the present study quantified the amount of high-intensity sound encountered over the previous 12 months, rather than lifetime exposure. Hence, it is likely that some listeners may have been classified as low NEB when, in fact, earlier high NEB already may have caused synaptopathy. Some listeners might have had high exposure to impulse noise that was not evaluated by the questionnaire for calculating NEB scores. The CBA/Caj mice in which noise-induced cochlear synaptopathy was first observed (e.g., Kujawa and Liberman, 2009) were raised in a laboratory setting enabling the researchers to efficiently control noise exposure. These animal experiments ruled out other forms of hearing deficit using the post-mortem cochlear synapse and cell counts. The noise exposure in human experiments cannot be controlled as efficiently as animal studies. In addition, the human experiments are usually limited to the non-invasive investigation of cochlear synapses that can limit their efficiency in identifying subtle changes in the synapses due to noise trauma. The ABR wave I amplitude is widely used to investigate cochlear synaptopathy in human studies (e.g., Valderrama et al., 2018; Paul et al., 2018; Bramhall et al., 2017; Le Prell and Clavier, 2017; Prendergast et al., 2017; Fulbright et al., 2017; Grinn et al., 2017; Guest et al., 2017; Yeend et al., 2017; Liberman et al., 2016; Stamper and Johnson, 2015a,b). However, it is essential to note that confounders such as head size (Trune et al., 1988) and high-frequency thresholds (Verhulst et al., 2016) may also influence the ABR amplitude. Therefore, the missing relationship between ABR wave I amplitude and NEB in our study cannot rule out the possibility of cochlear synaptopathy in noise-exposed young females.

It is also possible that humans have a better capacity for synaptic repair than the CBA/Caj mice strain in which noise-induced cochlear synaptopathy was first observed (e.g., Bayés et al., 2012). Comparable noise-exposure studies in guinea pigs showed that the synapse count largely recovers following an initial reduction due to noise exposure (Liu et al., 2012; Shi et al., 2016). The direct comparison of protein components from human and mouse excitatory synapses showed that the mouse and human postsynaptic density was comprised of around 1556 and 1461 proteins respectively. More than 70% of human and mouse postsynaptic density proteins were overlapping. Importantly, humans showed a significant abundance of some families of key postsynaptic density proteins including glutamatergic neurotransmitter receptors and adaptor proteins. The higher abundance of such protein contents associated with neural plasticity may provide increased synaptic plasticity to humans compared to rodents (Bayés et al., 2012). Humans also have considerable inter-individual variability in human synaptic proteins compared to laboratory rodents (Pinto et al., 2015), suggesting that there may be interactive effects between genetic susceptibility

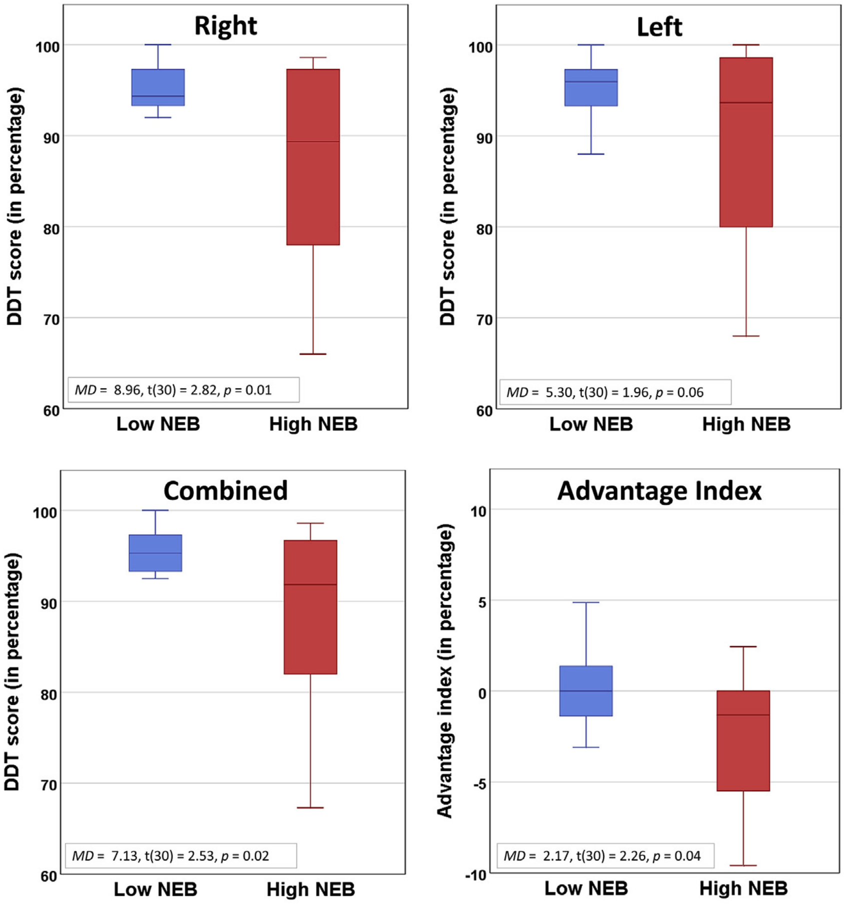

Fig. 4. Simple box plots for DDT scores between individuals with high NEB (red) and low NEB (blue). The performance of the right ear (top left), left ear (top right) and both ears (bottom left) for the free-recall condition are presented. The advantage index (bottom right) compares the right and left ear performance in the free-recall condition between high and low NEB groups. Independent *t*-test results are presented in the respective boxes. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

and environmental factors similar to noise-induced hearing loss (e.g., Abreu-Silva et al., 2011; Bhatt et al., 2016; Kowalski et al., 2014; Sliwinska-Kowalska and Pawelczyk, 2013). These factors might account, at least to some extent, for not observing a statistically significant difference for ABR wave I amplitude between individuals with high and low NEB (Yeend et al., 2017).

4.2. *Influence of high NEB on dichotic listening performance*

The present study documents the impact of high NEB on dichotic listening in a sample of noise-exposed young females with normal audiograms. NEB showed significant association with DDT$_C$ and DDT$_R$. NEB and DDT$_L$ did not achieve statistical significance (see Fig. 4). QuickSIN SNR loss was associated with DDT scores (DDT$_R$ and DDT$_C$), but NEB and QuickSIN SNR loss revealed no association. Similarly, no significant relation was observed between QuickSIN SNR loss, tinnitus, and SSQ12. However, the analysis revealed significant associations between DDT$_C$, tinnitus, and SSQ12. This observation suggests that DDT might be more sensitive to detect pathophysiological changes in the auditory system caused by high NEB compared to QuickSIN. Association between tinnitus and DDT$_C$ indicates the presence of a dichotic listening deficit, which may manifest as speech-in-noise difficulties in patients with tinnitus (Huang et al., 2007; Hennig et al., 2011; Ryu et al., 2012; Jain and Sahoo, 2014; Moon et al., 2015; Gilles et al., 2016; Tai and Husain, 2018).

The influence of high NEB on cortical neurons largely remains elusive. A few human studies compared mismatch negativity, an electrophysiological measure of sound discrimination ability of the cortical neurons, between noise-exposed workers and matched controls. The deviant-sound elicited mismatch negativity was larger to non-speech sounds than speech sounds in control subjects, while it did not differ between speech and non-speech sounds in the noise-exposed workers (Brattico et al., 2005). This observation suggests that long-term exposure to occupational noise could significantly influence sound discrimination ability by affecting the speed, strength, and topography of the neural auditory responses. It further indicates that subclinical changes in cortical responses to sounds may occur in subjects without peripheral damage but with continuous exposure to noisy occupational environments (Kujala et al., 2004; Brattico et al., 2005). Similar observations were made by the animal studies investigating the effects of long-term exposure to continuous non-traumatic noise (“assumed safe noise,” a Leq 8 h $\leq$ 80 dBA). These studies revealed that noise could modify neural processing in the midbrain, thalamus, and cortex in the absence of peripheral hearing loss, which may lead to sound processing deficit (e.g., Syka and Rybalko, 2000; see Eggermont, 2017 for the current discussion). It is plausible that high NEB modified the cortical neural responses to speech sounds resulting in the poorer DDT scores. Further research is needed to investigate the neurophysiological mechanisms underlying the relationship between NEB and DDT scores.

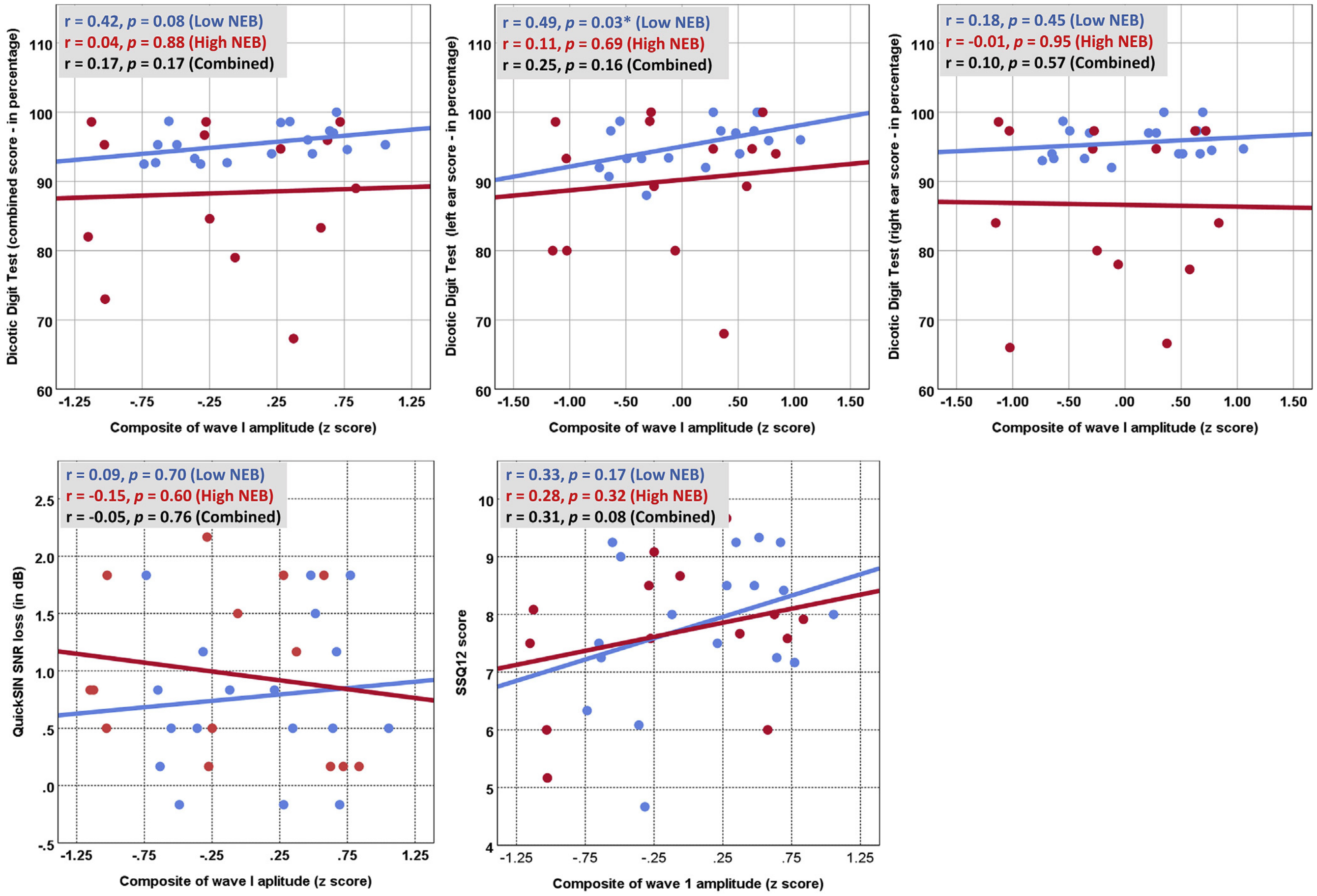

Fig. 5. Scatter plots between composite of wave I amplitude and DDT$_C$ (top left), DDT$_L$ (top middle), DDT$_R$ (top left), QuickSIN SNR loss (bottom left), and SSQ12 (bottom middle/right). The blue and red dots present results for individuals with low and high NEB, respectively. Linear regression lines were inserted to show the group-specific predictive relationship. Pearson's correlation coefficient (r) and *p* value are inserted on the top left corner. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

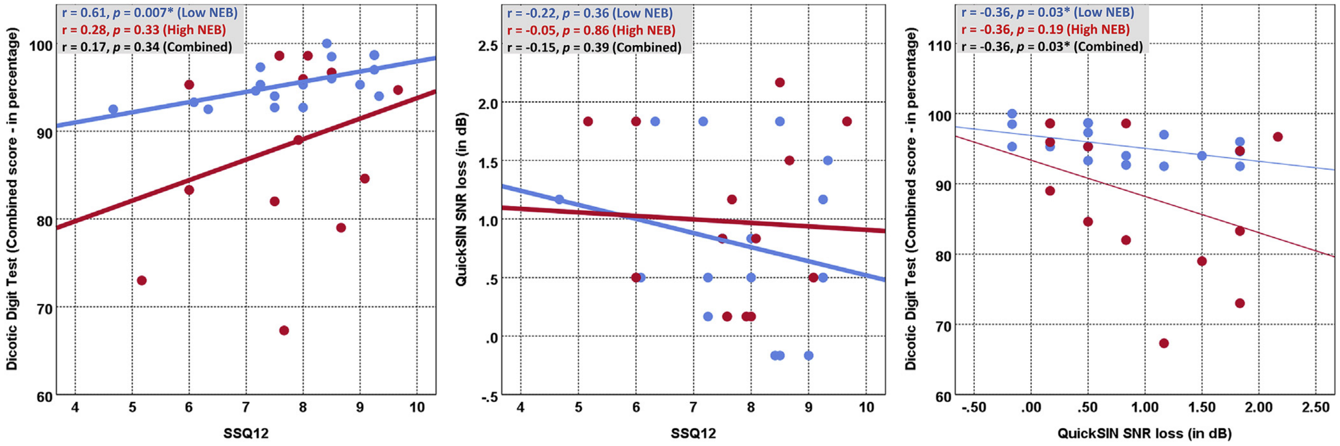

Fig. 6. Scatter plots for SSQ12 and DDT$_C$ (left), SSQ12 and QuickSIN SNR loss (middle), and QuickSIN SNR loss and DDT$_C$ (right). The blue and red dots present results for individuals with low and high NEB, respectively. Linear regression lines were inserted to show the group-specific predictive relationship. Pearson's correlation coefficient (r) and *p* value are inserted on the top left corner. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Performance on dichotic listening tasks can be influenced by auditory processing deficit in combination with attention and other supramodal processes, such as intelligence, working memory, and motivation (Moore et al., 2010). The cognitive influence on DDT performance in the present study cannot be ruled out, mainly because there is evidence to support that noise exposure adversely influences cognitive performance (Irgens-Hansen et al., 2015; Zeydabadi et al., 2018). Irgens-Hansen et al. (2015) studied visual attention in the noise-exposed Royal Norwegian Navy personnel. They found that the response time of the personnel with high noise exposure was significantly poorer compared to personnel with lower noise exposure. Zeydabadi et al. (2018) examined the cognitive performance of metal industry workers before and after the work shift. The workers with high noise exposure revealed significantly poorer selective attention, divided attention, selective response time, divided response time, and memory compared to workers with low noise exposure following a work shift. Similarly, Bressler et al. (2017) found that blast-exposed service members with normal to near-normal audiograms revealed speech-in-noise difficulties without showing a deficit in auditory brainstem neurons. The analysis of evoked potential revealed that the blast-exposed service members had weaker activation of frontal EEG channels and a failure of attention to enhance the neural responses for target sounds in the presence of distractors. The above evidence suggests that cognitive factors might have influenced the DDT performance of individuals with high NEB in the present study.

4.3. Influence of NEB on ear asymmetry

Most individuals report speech-related stimuli presented to their right ear with greater accuracy compared to their left ear in the free recall condition dichotic listening situation. This phenomenon is known as the right ear advantage (REA) which is observed in around 75–80% of right-handed individuals. Around 15–20% of right-handed individuals exhibit either no ear advantage or a left-ear advantage (LEA) (e.g., Bryden, 1988; Moncrieff, 2011). REA may be explained based on the neuro-anatomical model proposed by Kimura (1967). This model suggests that the crossed auditory pathways are stronger than the ipsilateral pathways, and during dichotic listening, the weaker ipsilateral pathways are additionally blocked or inhibited (Della Penna et al., 2006). Therefore, the auditory input from the right ear is directly conveyed to the relevant areas in the left hemisphere where speech processing takes place in most individuals. The input from the left ear is conveyed to the right hemisphere and then to the left hemisphere by the corpus callosum (Westerhausen and Hugdahl, 2008). Thus, dichotic listening can assess auditory function relying on the inter-hemispheric connection (Milner et al., 1968; Springer and Gazzaniga, 1975).

The present study found that individuals with high NEB showed significantly reduced REA ($\beta = -2.177$, $t(30) = -2.262$, $p = 0.031$, Fig. 4). The observation of reduced REA in the high NEB group is in agreement with Brattico et al. (2005), who studied mismatch negativity in normal hearing individuals. The study found that speech sound-elicited mismatch negativity was enhanced in the right hemisphere as compared to that of unexposed individuals. The authors noted that the enhanced response in the right hemisphere was found when noise was presented during the experimental session to individuals with no exposure to long-term noise (Shtyrov et al., 1998). The right hemisphere was more and the left was less involved in processing speech sounds in noisy rather than silent backgrounds (Shtyrov et al., 1998), which resembled the findings of Brattico et al. (2005). It was hypothesized that results observed in noise-exposed individuals derive from their long-term experience of hearing speech during work shifts in the presence of a noisy background, thus resulting in the generally enhanced role of the right-hemisphere in speech processing also observed in silent listening conditions (Kujala and Brattico, 2009). The present study supports Brattico's hypothesis.

Physiological interpretation of asymmetry in dichotic listening is open for debate. The most common interpretation suggests that LEA for verbal stimuli indicate mixed or right hemisphere dominance for language that is a common finding among children with phonologic, reading, language and learning disorders (Kimura, 1961; Hugdahl, 2004; Newman and Sandridge, 2007). However, validation studies suggest that REA is a valuable predictor of left-hemisphere dominance, but LEA is not as predictive of right-hemisphere dominance. It can be hypothesized that high NEB might change the hemispheric lateralization resulting in an enhanced role of the right hemisphere in dichotic listening. This hypothesis further suggests that exposure to high NEB in early childhood might result in changes in the hemispheric lateralization that may be a contributing factor for phonologic, reading, language and learning disorders. Another possible interpretation comes from a neuroimaging study which found that LEA was associated with increased axial diffusivity in the left internal capsule (including projections to the auditory cortex), and decreased functional activation in the left frontal eye fields (i.e. an area known for regulating attention) compared to REA (Schmithorst et al., 2013). Therefore, it can be argued that both sensory and attentional deficits may be predictive of LEA in individuals with high NEB. Further research is required to investigate the effect of NEB on advantage index to delineate the neurophysiological substrates.

4.4. Experimental caveats

The results of the present study cannot be generalized on males. Additionally, the present study was limited by its survey design to estimate NEB. Although NEB was estimated using a validated survey tool, measurements using a comprehensive battery of noise dosimetry would yield greater precision. The questionnaire did not include an exhaustive list of noise exposure areas and did not account for the use of ear protection in the process of calculating NEB score. Even though there is no widely accepted “gold standard” for evaluating cochlear synaptopathy in humans, it can be argued that electrophysiological protocols other than the one employed by the present study might be more sensitive in identifying cochlear synaptopathy in humans (e.g., Mehraei et al., 2016). It is plausible that noise exposure can cause cognitive decline, and the cognitive factors may play a role in the dichotic listening performance. However, the present study did not evaluate cognitive tests on these subjects. Finally, the relation between the advantage index and NEB should be replicated in independent investigations.

5. Conclusions

NEB showed no association with behavioral hearing thresholds, DPOAEs, ABR measures, and speech-in-noise performance. Individuals with high NEB, lower SSQ12 scores and tinnitus perception revealed significantly lower DDT_C scores. Individuals with high NEB showed lower values of advantage index compared to individuals with low NEB. These results suggest that young females with high NEB might reveal dichotic listening deficits prior to showing changes in QuickSIN performance and ABR wave I amplitude.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heares.2019.05.008.

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