Lateralized and Sex-Specific Effects for a Relationship between the MOC Reflex and Response Time to Auditory Events in Noise

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Abstract

Objective: The objective of the study was to quantify the relationship between the medial olivocochlear (MOC) reflex and auditory perception in noise, and to evaluate the influence of ear and sex on this relationship.

Design: MOC activity was measured from each ear of samples of female and male subjects by recording the inhibition of click evoked otoacoustic emissions (CEOAE) induced by contralateral broadband noise at 60 dB SPL. The response times for verbal and nonverbal stimuli presented in quiet and with contralateral broadband noise were used to document auditory perception.

Study sample: Twenty participants with normal hearing, (10 males, 10 females) took part in the study.

Results: Robust sex differences were observed for the CEOAE amplitudes in quiet, with contralateral noise and for the auditory perception in noise listening tasks. Females showed larger CEOAE inhibition compared to males, and also faster response times to auditory stimuli in noise. The main effect of stimuli type on response time was significant when controlling for the variance of left ear inhibition, but disappeared when controlling for the inhibition of the right ear CEAOE.

Conclusion: The magnitude of the MOC reflex and the perceptual response time to auditory stimuli are correlated, with stronger effects for females, compared to males. This suggests a functional relationship between the MOC reflex and response time to auditory stimuli, and that peripheral lateralization of the auditory system can be associated the lateralized auditory perception at the cortical level.

Keywords: Auditory perception; noise; COAE; efferent MOC inhibition

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Introduction

The present study focuses on the mechanism underlying efferent control of the cochlea and peripheral processing of auditory stimuli, and how these mechanisms mediate the perception and interpretation of auditory signals in noise. Despite having to extract and decode relevant auditory information from a complex mixture of acoustic signals, the normal human auditory system is quite successful at speech in noise perception (Kim, Frisina, Mapes, Hickman, & Frisina, 2006). For instance, we can attend to a single voice even when many people are talking simultaneously. This phenomenon is often referred to as the "cocktail party" effect (Pollack & Pickett, 1957), but is also related to what has been termed “auditory scene analysis” (Bregman, 2005). In order to carry out a meaningful conversation in such circumstances, one needs to be able to extract the specific information that is sent from the respective communication partner, while the speech of others must be ignored. Previous research has suggested a role of the corticofugal system in the "top-down” processing (cortex-cochlea) of auditory information, and has also suggested a role in auditory perception and attention in noise (de Boer & Thornton, 2007; DeBonis & Donohue, 2004; Khalfa et al., 2001).

A large body of research in experimental animals suggests that the olivocochlear efferent auditory nervous system serves a role in the neural processing and perception of signals in background noise (Guinan, 1996, 2006; May, Budelis, & Niparko, 2004; D. W. Smith, Turner, & Henson, 2000). One specific efferent neural circuit believed to be involved in noise suppression at the level cochlea is the medial olivocochlear (MOC) bundle. The uncrossed MOC bundle consists of neurons with large cell bodies in the superior olivary complex that receive innervation from axons originating in the contralateral cochlear nucleus, and whose axons project to outer hair cells (OHCs) within the ipsilateral cochlea (see figure 1 in Guinan, 2006). Activation of the uncrossed MOC bundle, either by direct electrical stimulation (Gifford & Guinan, 1987) or by presenting steady state noise to one ear (Berlin, Hood, Hurley, & Wen, 1994; Berlin et al., 1993; Hood, Berlin, Hurley, Cecola, & Bell, 1996; Liberman, 1989) makes OHCs in the opposite ear less excitable by increasing membrane conductance. Because OHCs are the putative generators of the cochlear amplifier, activating the MOC bundle decreases the gain of the cochlear amplifier; this is known as the MOC reflex (MOCR).

It is possible to study the MOCR non-invasively in humans using click-evoked otoacoustic emissions (CEOAEs). CEOAEs are small acoustic waveforms produced by the cochlea and recorded in the ear canal when brief sounds are presented to ears with normal OHC function; presumably, CEOAEs are generated by the coherent reflection of cochlear traveling wave energy from changes in OHC stiffness along the basilar membrane (Shera & Guinan, 1999). The CEOAEs are also frequently referred to as Transient Evoked Otoacoustic emissions (TEOAE, Froehlich, Collet, & Morgon, 1993; Glattke & Robinette, 2007). In the *contralateral inhibition of CEOAEs* technique, CEOAEs are recorded first in quiet and then with noise presented to the opposite ear, which activates the MOCR. The amplitude differences between CEOAEs recorded in quiet and with contralateral noise are used to quantify attenuation of the cochlear amplifier mediated by the MOCR. The amount of CEOAE inhibition with MOC activation typically ranges from 1-2 dB overall in normal hearing listeners and is most evident in the cochlear tonotopic frequency range of 1-4 kHz (Berlin et al., 1994; Velenovsky & Glattke, 2007; Wagner & Heyd, 2011).

With respect to the current study, two important findings have been reported in the human MOC reflex literature. The first is that *the magnitude of contralateral CEOAE inhibition may be positively correlated with signal- and speech-in-noise perception* (Giraud, Garnier, et al., 1997; Kumar & Vanaja, 2004; Micheyl & Collet, 1996; Micheyl, Morlet, Giraud, Collet, & Morgon, 1995; Yilmaz, Sennaroglu, Sennaroglu, & Kose, 2007). This relationship suggests that the efferent auditory system is involved in filtering and inhibition of background noise at the level of the inner ear and that the activity of the MOCR may impact perception, although not all studies support this claim (Garinis, Werner, & Abdala, 2011; Wagner, Frey, Heppelmann, Plontke, & Zenner, 2008).

The second finding is that *cochlear mechanics may be influenced by attention* in adults, suggesting that the cortex is able to modulate the MOC reflex via efferent neural tracts (Abdala, Dhar, Ahmadi, & Luo, 2014; Avan & Bonfils, 1992; deBoer & Thornton, 2007; Garinis, Glattke, & Cone, 2011; Maison, Micheyl, & Collet, 2001; Mishra & Lutman, 2014; Perrot et al., 2006). Thus, the efferent system may be recruited during active listening to exert a cortical top-down influence *in real time* to selectively enhance or suppress incoming auditory information at multiple subcortical sites. It remains unclear if task difficulty influences the degree to which the cortex modulates this reflex (S. B. Smith & Cone, 2015). Understanding how attention influences early auditory processing in normal listeners is critical, as speech-in-noise deficits may reflect an inability to cognitively engage the efferent auditory system (Muchnik et al., 2004). For example, individuals with disordered auditory processing (APD), who often experience difficulty perceiving speech signals in background noise, show a lower OAE inhibition compared to people without such processing deficits (Burguetti & Carvallo, 2008; Yalcinkaya, Yilmaz, & Muluk, 2010).

It is well accepted that there are cerebral hemispheric differences in auditory function. For example, the left hemisphere dominates the processing of linguistic material, while music and nonverbal stimuli mainly recruit right brain resources (Hugdahl, 2003; Kimura, 1961, 1967; Zatorre, 2003). This laterality appears to be preserved at the level of the auditory periphery with larger spontaneous otoacoustic emissions (SOAE) and TEOAE in the right ear (Bright, 2007; Sininger & Cone-Wesson, 2004), greater OAE inhibition or MOC activation in the right ear (Khalfa & Collet, 1996; Khalfa, Micheyl, Veuillet, & Collet, 1998), as well as a faster and more accurate gap detection when noise bursts are presented in the right ear (S. Brown & Nicholls, 1997).

People with APD have also difficulty performing a directed attention task (Hugdahl et al., 2009), on dichotic listening with CV-syllables (DLCV). In particular, the forced left task as it is described in the forced attention paradigm for dichotic listening tests (Hugdahl & Andersson, 1986). The ability to perform the forced attention tasks in dichotic listening is related to *suppression* of TEOAE (Markevych, Asbjørnsen, Lind, Plante, & Cone-Wesson, 2011).

Kim, Frisina and Frisina (2006) reported that speech perception in noise, as assessed with the hearing in noise test (HINT), shared variance with degree of *DPOAE suppression*. The most significant correlations were found for DPOAE frequencies 1-2 kHz, which represents a range that is important to speech perception. A study carried out by Giraud et al. (1997) also showed correlation between *degree of OAE suppression* and the ability to recognize words that were presented in the noise.

Sex differences are frequently found in both spontaneous otoacoustic emissions and in CEOAEs (Mcfadden, 1993; Mcfadden & Loehlin, 1995), with higher frequencies of SOAE in females compared to males, as well as in inhibition of CEOAES (Velenovsky & Glattke, 2007). Hearing loss following noise exposure is also reported to be lateralized and gender specific, with higher susceptibility of hearing loss for left ear in males (Berg, Pickett, Linneman, Wood, & Marlenga, 2014). In addition, Markevych, Asbjørnsen, Lind, Plante and Cone (2011) reported gender differences in inhibition of the MOCR, and also gender dependent differences in patterns of correlations between the MOCR and measures of auditory perceptions. These differences will be further investigated in the present study.

Purpose and Hypotheses

It appears that the MOC reflex, a bottom-up afferent-efferent loop is involved in the ability to hear speech in noise, and also that top-down corticofugal pathways can modulate the MOC reflex. In this study, we measure the ability to hear speech in noise and also the magnitude of CEOAE inhibition, replicating and extending the work of Kim et al. (2006). We tested two hypotheses: first, that the magnitude of CEOAE inhibition would be correlated with the accuracy and response time for perceiving signals in noise. Second, that speech and noise abilities would demonstrate sex and ear differences similar to those found for CEOAE inhibition, specifically that right ear performance would be better than left ear performance, and female performance would exceed that for males.

Method

Participants

The sample consisted of ten males and ten females (all right-handed) with an average age of 24 years in both groups (age range 19-29 years). Participants were recruited using information posted at the premises associated with the University of Bergen.

Criteria for participation were normal pure tone hearing threshold in both ears (< 20 dB HL for 250-8000 Hz), no known neurological diseases, and no use of drugs that are known to affect hearing, such as quinine, diuretics, aspirin, or benzodiazepines (Morand-Villeneuve et al., 2003; Sun et al., 2009). Because previous research has found temporary reduction in hearing threshold following exposure to high level noise, such as nightclubs or concerts (Engdahl, Woxen, Arnesen, & Mair, 1996), the participants could not have been exposed to such noise within the last 24 hours before testing. Participants were tested with the Bergen dichotic listening test with consonant-vowel syllables, the DLCV-108 dichotic listening test (Hugdahl & Asbjørnsen, 1994) for control of auditory perception, lateralization and attention. The DLCV-108 consists of six CV-syllables including the six stop consonants /b/, /d/, /g/, /k/, /t/ and /p/ paired with the vowel /a/. The CV-syllables are combined in all possible combination to create 36 pairs of syllables (including the homonymic pairs). Three different pseudorandomized lists of syllables are used for the test. Each list is presented with a different instruction. The first list is always done with an instruction to report the syllable that is perceived most clearly thus emphasizing free report, but also encourage single syllable responses. This free recall procedure is commonly referred to the "Non-forced task" (NF). The two following lists are presented with either an instruction to attend to the right ear and report the syllable heard in the right ear, or to attend to the left ear and to report the syllable heard in the left ear. These tasks are referred to the "Forced Right" (FR) or the "Forced Left" (FL) tasks according to the "Forced attention paradigm" of dichotic listening tasks (Hugdahl & Andersson, 1986). To be included in the study they were required to demonstrate normal results for the dichotic listening tasks, defined as a right ear score higher than the left ear score during free reporting (the non-forced task) and also to demonstrate attention modulation of the responses in forced right (FR) and forced left (FL) conditions (Westerhausen, Bless, Passow, Kompus, & Hugdahl, 2015).

All subjects were required to demonstrate the presence of CEOAEs for a 60 dB peSPL *non-linear* click stimulus in each ear. CEOAEs were considered to be present if the response could be measured with SNR > 6 dB in the frequency bands from 1.0 to 5.0 kHz, and have a "whole-wave" reproducibility value of greater than 75%.

Six additional volunteers did not meet the criteria for participation: one female showed no recordable OAE at 60 dB, even though normal hearing was indicated the by pure tone threshold test. One female had pure tone thresholds that exceeded 20 dB at 1500 and 2000 Hz for the right ear. Two male and two female participants showed lack of attention modulation for the DL test. All participants received NOK 100 (approximately 15 US dollars) as compensation for participation in the study.

Hand Preference

Hand preference was documented using a Norwegian version of the questionnaire of hand preference prepared by Raczkowzki, Kalat and Nebes (1974). Each activity carried out with the right hand was awarded 1 point, of which the maximum score was 15 points, indicating all 15 tasks would be habitually performed by right hand and thus complete right handedness. A minimum score of 0 would indicate complete left handedness. Right handedness was defined as at least 12 of the 15 tasks were habitually performed with the right hand.

Measurement of the MOCR: CEOAE and CEOAE Inhibition

An Otodynamics ILO-292 USB II system with ILO V6 clinical software (Otodynamics Audiology Systems, 2011) was used to record the CEOAE in both ears. ILO-292 probe was placed in the external ear canal and *linear* click stimuli of 60 dB peSPL were presented to evoke CEOAEs. Only those participants who had identifiable CEOAE at 60 dB were further tested for contralateral inhibition effects. The ILO v6 software (Otodynamics Audiology Systems, 2011) also presented the contralateral, and OAEs were recorded during alternating conditions of quiet and contralateral broadband noise (BBN) at 60 dB SPL. The duty cycle of the noise was 3 s. Differences between the CEOAE amplitude in quiet vs. contralateral noise can thus be ascribed to this activation of the MOCR. Each response was averaged over 260 sweeps, or a total of 2048 clicks. The participants were instructed to sit still during the CEOAE measurement to avoid movement artefact.

Perception in Noise Experiment

Perception in noise entailed asking listeners to identify verbal and nonverbal stimuli presented monaurally through a Creative lab THX Sound Blaster 1240 sound card with AKG acoustics K141 head phones with noise at 60 dB SPL. All sounds were presented with noise at 60 dBSPL and 0 dB SNR. *The verbal tokens* consisted of the six CVs from the DLCV-test: /ba/, /da/, /ga/, /pa/, /ta/ and /ka/, with token durations of 360-500 ms. Note that the stop consonants that are used for the syllables are produced in three different locations (bilabial, velar and alveolar) and also either voiced or unvoiced, and combined with the vowel /a/. They are sound patterns that are easily recognized in isolation and occur frequently in many languages. A new token was presented one second following the response to the former. Four seconds response time was allowed for before the trial was skipped as a no response trial and the program continued with the net trial. All six syllables were visible on a computer screen in fixed order during each auditory syllable presentation as a forced choice task. The response chart served as the response sheet for the task. The participants were instructed to respond as quickly as possible on each trial using a mouse click on the token indicating the syllable they heard. During practice trials without noise, 100 % correct was achieved for all syllables, and there was no difference in response time to the different syllables.

The nonverbal tokens, consisted of recordings of two human nonverbal sounds (baby laughter; coughing); two animal sounds (cat meow; rooster crow); two musical instruments (guitar strum, a tin whistle scale). Each token was of 1000 ms duration, and the sound files were edited to the same average amplitude. The non-verbal tokens were chosen as they are expected to be preferably processed by the right cerebral hemisphere as opposed to the left sided preference for the CV-syllables (Hugdahl et al., 1999). Immediately after the sound file exposure a response chart containing six boxes with an image of the objects producing the sounds was presented. A new token followed one second after the response was given to the former token. Otherwise the procedure was identical to the procedure for the verbal stimuli. During test trials without noise, the accuracy score was 100 %, and there were no differences in response time to the different nonverbal tokens.

Tokens were presented alternately to the right and left ear in random sequences in a block design, with alternating blocks of verbal and nonverbal tokens. The response time for each correct response was recorded.

Broad band noise was delivered by the computer from the E-Prime program and the output was calibrated to 60 dB SPL, as were the verbal and non-verbal auditory tokens. There were three conditions for the perceptual recognition tasks, no noise (NN), noise left (NL) and noise right (NR). The first condition was a no-noise condition, in which tokens were presented monaurally without ipsilateral or contralateral noise. For the noise left condition BBN was presented continuously to the left ear while the target tokens were presented randomly to the left or right ear. During the noise right condition, the broadband noise was delivered continuously to the right ear, and target stimuli, both verbal and nonverbal, were presented randomly to the right or the left ear.

Presentation of verbal and nonverbal stimuli was blocked, with 12 randomly presented stimuli in each block. Noise conditions were changed randomly between each block. Eight blocks of stimuli were presented during each of the noise conditions, a total of 24 blocks of trials. However, only no noise and contralateral noise trials were used for the analyses. That is, trials in which the tokens were presented to the ear with the noise were not included.

The calibration of tokens and noise was done using a Bruel & Kjær head and torso simulator (HATS) type 4128 C with a Bruel & Kjær sound level meter Type 2250 attached.

The response time and accuracy were recorded by the computer program as the time in milliseconds from stimulus presentation to the mouse click response. The response was recorded as an error if the button was not clicked on the correct picture and the response time was in this context recorded as an invalid trial and was excluded from the result. If there was no response during the 4 seconds response interval, it was recorded as an erroneous trial.

The experimental protocol and recording of responses were programmed in E-Prime version 2.0 (Schneider, Eschman, & Zuccolotto, 2007)

Procedure

On arrival in the lab, the participant's hand preference was determined, and pure tone thresholds were measured. Participants who meet the criteria for normal hearing threshold (≤ 20 dB HL) were further tested for CEOAE responses in each ear by using click stimuli of 60 dB peSPL. If CEOAE responses met the criteria, CEOAE inhibition was tested. CEOAE amplitude was calculated in the ILO v6 software as the mean of the A+B buffers, in dB rms. Participants then went through the dichotic listening test. After the DL test, the perception–in-noise experiment was carried out. The procedures took about 75 minutes to complete.

Data Analyses

Multifactorial analysis of variance (mixed ANOVA) was used to calculate effect sizes and group differences between the independent variables in accordance with the experimental design. Analysis of covariance (ANCOVA) using CEOAE inhibition for left and right ears was used to control for the shared variance in effect sizes. Fisher's LSD test were completed on all significant ($p < .05$) effects involving more than two means, and post hoc tests were executed both before and after the inclusion of covariates in the analysis. We also used Pearson product-moment correlation analyses to examine the strength of the correlation between CEOAE inhibition, OAE laterality index (LI) and auditory perception in noise.

CEOAE inhibition was calculated as follows:

Formula 1: $$CEOAE_{inhib} = CEOAE_{NN} - CEOAE_{CN}$$

where NN represents No Noise and CN represents Contralateral Noise. The laterality index (LI) for OAE was calculated using the formula:

Formula 2: $$LI_{OAE} = \left(\frac{RE_{OAE} - LE_{OAE}}{RE_{OAE} + LE_{OAE}}\right) * 100$$

The result of such a calculation describes the relationship between the OAE of right (RE) and left (LE) ear as a percentage score, where positive values refers to a right ear advantage (REA) and negative values indicates a left ear advantage (LEA).

The data from the perception in noise experiment was analysed in similar ANOVA designs, using the number of correct reports from each condition and the response time in milliseconds as dependent measures. Similarly, the dichotic listening performance was analysed based on the number of correct reports from each ear during the three attention tasks.

Statistica version 64 version 10 (StatSoft Inc., 2011) was used for all statistical analyses.

Results

Table 1 summarizes the mean values for 16 variables, including age, sex, handedness, CEOAE amplitude, CEOAE inhibition, CEOAE laterality, and 7 dichotic listening variables (see table legend). There were no differences in age or handedness score between the male and female subjects. The results for CEOAE and DL tests are explained below.

Table 1 Mean Scores for the Variables Included in the Study, In Addition to Background Variables of Age and Hand Preference separate for the Male and the Female Participants

	Males		*Females*	
	Mean	*Sd*	Mean	*Sd*
Age	24.0	*3.4*	24.2	*3.9*
Handedness, tasks performed with right hand	12.5	*2.1*	13.2	*2.2*
$OAELE_Q$ dB	5.8	*3.0*	8.8	*2.6*
$OAERE_Q$ dB	7.5	*2.8*	9.8	*2.2*
$OAELE_N$ dB	5.2	*2.8*	7.6	*2.8*
$OAERE_N$ dB	6.7	*3.0*	8.4	*2.5*
$Inhibition_{LE}$ dB	0.7	0.6	1.2	0.5
$Inhibition_{RE}$ dB	0.8	0.6	1.4	0.4
OAE_{LI}	14.8	*15.8*	6.4	*10.5*
DLNFLE. correct items	12.2	*4.8*	9.2	*2.6*
DLNFRE, correct items	14.5	*4.5*	17.2	*2.4*
DLFRLE, correct items	9.0	*3.2*	6.7	*2.8*
DLFRRE, correct items	18.8	*4.1*	21.1	*3.5*
DLFLLE, correct items	15.8	*5.1*	17.9	*4.5*
DLFLLE, correct items	10.7	*5.3*	9.2	*3.5*
DL_{LI}	9.1	*32.6*	30.5	*18.8*

Note: $OAELE_Q$ = Otoacoustic emission for left ear in quiet; $OAELE_N$ = Otoacoustic emission for left ear with contralateral noise; $OAERE_Q$ = Otoacoustic emission for right ear in quiet; $OAELE_N$ = Otoacoustic emission for right ear with contralateral noise; OAE_{LI} = Laterality index for the otoacoustic emissions; DLNFLE = Dichotic listening score for the left ear during the Non-Forced Task; DLNFRE = Dichotic listening score for the right ear during the Non-Forced Task; DLFRLE = Dichotic listening score for the left ear during the Forced Right Task; DLFRRE = Dichotic listening score for the right ear during the Forced Right Task; DLFLLE = Dichotic listening score for the left ear during the Forced Left Task; DLFLRE = Dichotic listening score for the right ear during the Forced Left Task; DL_{LI} = Laterality index for the Non Forced Dichotic Listening Task

CEOAE

The results of the initial CEOAE test given (in quiet) to qualify a listener for the experimental study were analysed for ear and sex differences. The mean amplitudes for right and left ears for male and female subjects are shown in Table 1. As expected, females had larger CEOAEs than males by about 2 dB, and right ear CEOAE amplitudes were larger than for the left by about 1.0 or 1.5 dB. A two-way ANOVA in which ear (right vs. left) was treated as a repeated measure and sex (male vs female) as an independent variable was completed. Statistically significant ear and sex effects were found, as the CEOAE was generally stronger for right ear compared to the left ear ($F_{(1, 18)} = 14.08, p < .001, \eta^2 = .44$), and male participants demonstrated larger amplitude responses compared to males ($F_{(1, 18)} = 5.31$ $p = .033, \eta^2 = .23$).

CEOAE Inhibition -- MOCR

The values shown for the CEOAE MOCR test (Table 1) indicate the mean amount of inhibition in dB (amplitude in no noise minus the amplitude with contralateral noise) for males vs females and right vs. left ear. As in the no noise condition, there appears to be an advantage for females and right ear. CEAOE inhibition was analysed with the same two-way design used for CEOAE in quiet but with an added repeated measurement variable of noise vs. no noise. The analysis yielded a significant main effect for Ear ($F_{(1, 18)} = 4.56, p = .046, \eta^2 = .20$), with larger inhibition for the right ear compared to the left ear on the order of 0.1-0.2 dB. Sex yielded a significant main effect ($F_{(1, 18)} = 7.45, p = .013, \eta^2 = .29$) as females showed a significantly larger inhibition than males, that is, by a factor of 2.

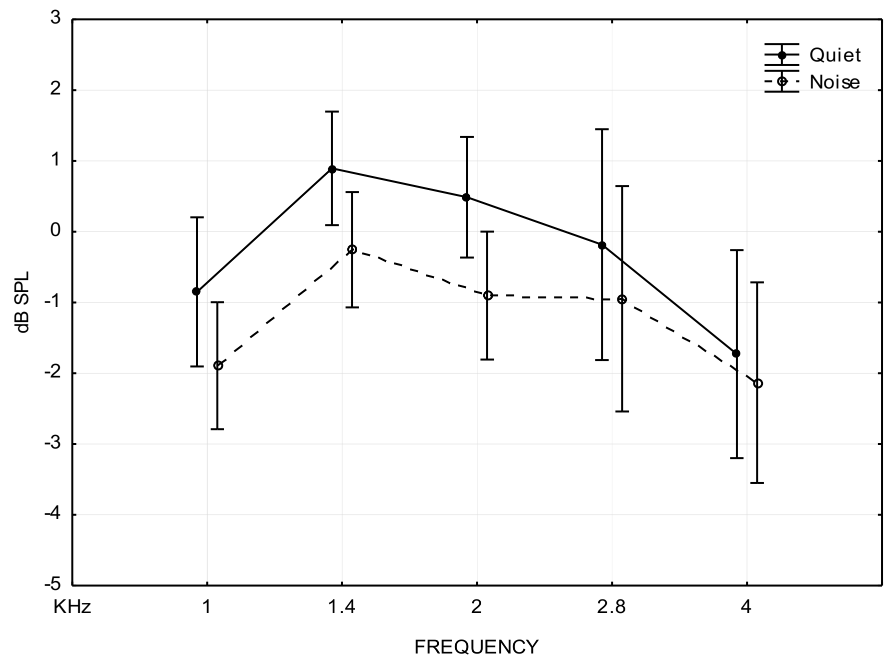

Figure 1. Mean CEOAE in dB SPL as recorded for the frequency bands 1, 1.4, 2, 2.8 and 4 kHz in quiet and with contralateral noise. Small bars indicate +/- 1 SE

MOCR strength by Frequency Band

The MOCR strength of CEOAEs was further analysed by measuring the amplitude in frequency bands centred at 1.0, 1.4, 2.0, 2.8 and 4.0 kHz (see Figure 1). Males demonstrate a "peak" in the amplitude by frequency plots, whereas, the females have a flatter configuration to this function. For males, the largest CEOAE amplitudes were observed in the 1.4-2.0 frequency bands for both ears. Females have a slightly rising contour to the CEOAE amplitude by frequency plot for the left ear, but it is relatively flat for the right ear. These contour differences are observed in the contralateral noise (MOCR activated) condition as well, except for the right ear of females for which there is a slight dip at 2.0 kHz, indicating greater inhibition in the frequency range. An additional four way ANOVA was conducted using frequency bands, noise conditions and ear as repeated measurements within subjects and sex as a between groups factor. The analysis yielded a main effect of Ear [$F_{(1, 18)} = 11.29$, $p > .005$, $\eta^2 = .39$], with over all stronger emissions elicited from the right compared to the left ear. Also there was a robust main effect of noise condition, [$F_{(1, 18)} = 90.25$, $p < .001$, $\eta^2 = .75$] as expected. Finally, there was a sex effect, as females yielded larger emissions compared to males independent of the presence of contralateral noise [$F(_{1, 18}) = 7.22$, $p < .05$, $\eta^2 = .29$].

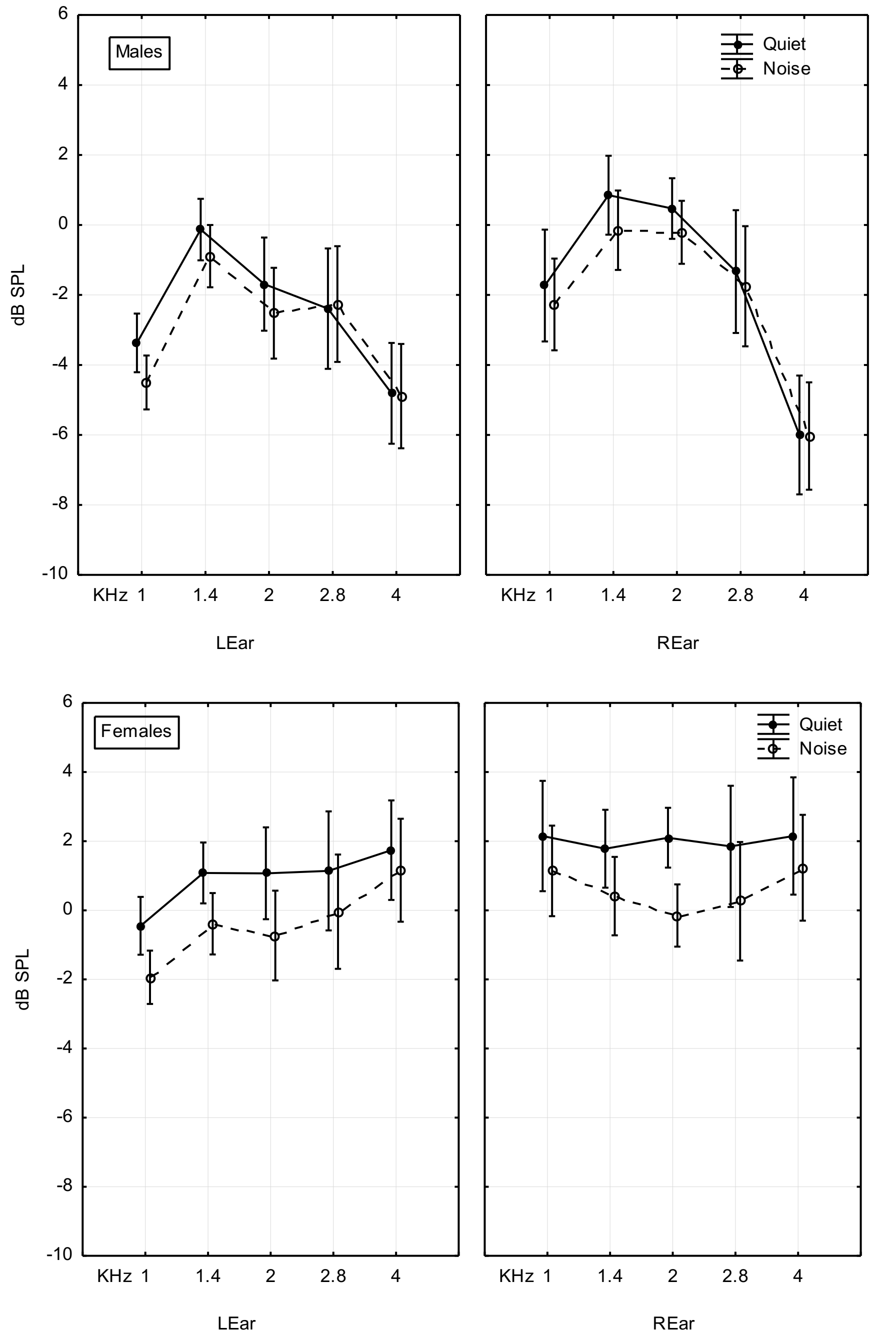

Figure 2. Mean CEOAE in dB SPL as recorded for the frequency bands 1, 1.4, 2, 2.8 and 4 kHz, separate for male (upper panels) and female (lower panels) participants during quiet and with contralateral noise, separate for left (Lear) and right (Rear) ear. Small bars indicate +/- 1 SE

Sex also yielded an interaction effect with emissions during the different noise conditions [$F_{(1, 18)} = 12.55, p < .005, \eta^2 = .41$]. *Tukey's HSD* test as post hoc test revealed that the effect could be explained by over-all larger effect of the noise among the female participants compared to the males. Sex also yielded an interaction effect with emissions of the different frequency bands [$F_{(4, 72)} = 3.07, p < .05, \eta^2 = .15$]. *Tukey's HSD* test revealed that the interaction could be explained by lower emissions in the male participants at the lower (1.0 kHz) and the higher (4.0 kHZ) frequency bands, but not in the middle frequencies. Finally, the analysis also yielded an interaction between noise condition and frequency bands [$F_{(4, 72)}$ = 6.06, p < .001, η^2= .25]. Follow up with *Tukey's HSD* test revealed that there were significant differences for the lower frequency bands (1.0-2.0 kHz), but not for the higher frequencies (see Figure 2). No other sources of variance yielded significant effects.

Dichotic Listening Performance

The results of the dichotic listening test given to qualify participants for this study are summarized in Table 1, and are also depicted in Figure 3. Females showed a mean right ear advantage (DL laterality index) of 30.5 % for compared to a score of 9.1% for males. The forced ear listening results demonstrate very different performance for female and male listeners. Females had scores of 74.1 % and -20.8 % for in FR and FL respectively, whereas males had scores of 44.3 % and -5.6 % in the same conditions. There is a greater than 90% difference between FR and FL scores for females, but only a 50% difference for males. These sex-related differences in laterality are depicted in Figure 3 that presents scores for non-forced and forced listening conditions, separated by sex, with ear as the parameter. The differences in performance as a function of ear and sex were subjected to a three way ANOVA, in which task (NF, FR, FL) and ear (right vs. left) were treated as repeated measures within subjects and sex (male vs. female) was treated as a between groups factor. The analysis yielded, as expected, a robust ear-effect [$F_{(1,18)}$ = 8.17, p < .05, η^2 = .31], in addition to a strong ear by task interaction effect that reflects the ability of both females and males to do follow the instructions of the attentional tasks and show attentional modulations [$F_{(2, 36)}$ = 41.30, p < .001, η^2 = .70]. No other sources of variance yielded significant effects. However, when inspecting the mean scores for the dichotic test performance by male and female participants, there appears to be better performance for the female participants (see Figure 3), which is also suggested by earlier studies (Markevych et al., 2011). To further investigate the gender specific scores, we conducted a series of pairwise t-tests for specific contrasts of interest. These analyses revealed that in spite of non-significant interactions involving sex, the male participants showed no significant REA during the NF task, while the females showed a significant REA. In addition, the males also failed to show an expected inhibition of the right ear score when comparing the NF and the FR tasks, while this inhibition effect was evident for the females (p < .001). Male participants yielded a larger variability compared to females for the Laterality index (LI) ($SD_{females}$ = 16.62, SD_{males} = 30.10, $F_{(variance)}$ = 3.28, p = .006).

Perception in Noise Experiment

Reaction times were analysed for perception of verbal and non-verbal tokens were measured in quiet and in noise, for right vs. left ear presentations, and for male vs. female listeners. These are summarized in Table 2. In quiet conditions, the mean reaction time for verbal stimuli was shorter for females compared to males, and for *left* ear presentation compared to right. Reaction times for non-verbal stimuli were shorter than those for verbal stimuli, and shorter for right ear compared to left in both females and males. In the contralateral noise condition with verbal stimuli, females also had shorter reaction times than males but there did not appear to be an ear difference. Non-verbal stimuli evoked longer reaction times in men for the left ear, compared to the left ear of females, but there was very little difference in male vs. female reaction times for the right ear.

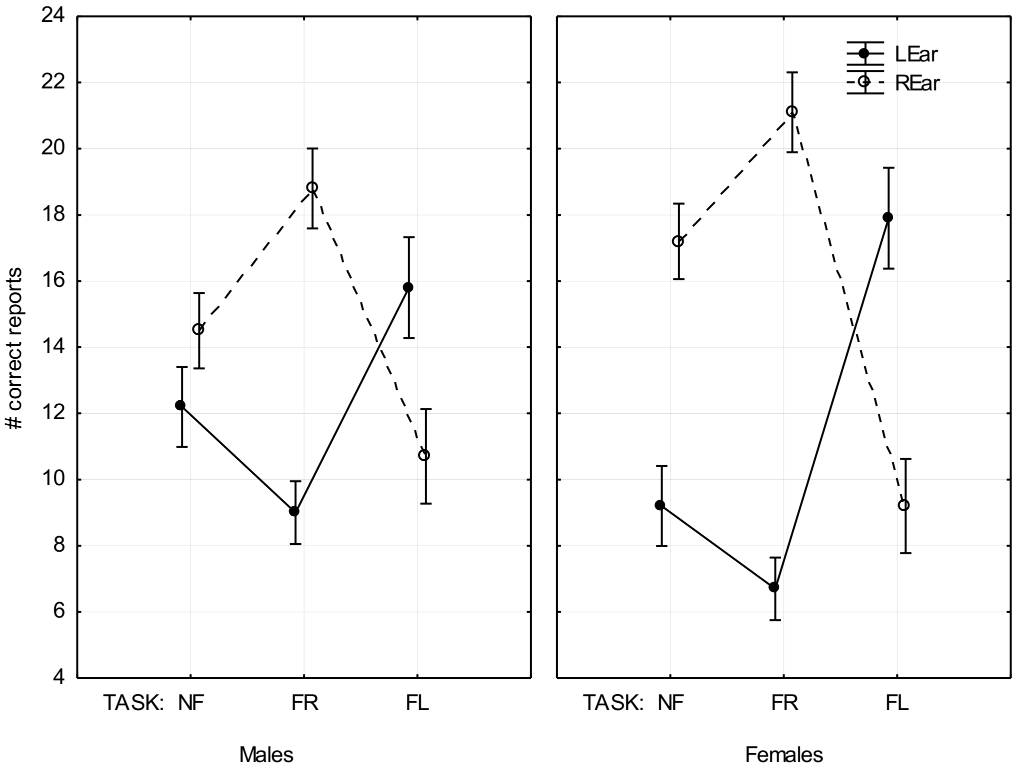

Figure 3: Number of correctly reported syllables during the dichotic listening test, separate for right (Rear) and left ear (Lear) during the performance of the three attentional tasks, non-forced (NF), forced right (FR) and forced left (FL). Male participants in the left hand panel; female participants in the right hand panel. Error bars in the graph represents +/- 1 SE

The reaction times for sex, ear, noise condition and type of stimulus can be visualized in Figure 4. These reaction times for correct responses were analysed with a 4-way ANOVA, where sex was treated as a between groups factor, and the noise condition (NN vs. CLN), ear (R vs. L) and stimulus (verbal vs. non-verbal) three variables as repeated measurements within subjects. The analysis yielded no significant main effects for any of the variables in the design. Yet, there were two significant two-way interaction effects: Noise by Sex [$F_{(1,18)}$ = 9.84, p = .005, η^2 =.35] and Ear by Stimulus [$F_{(1,18)}$ = 8.76, p = .008, η^2= .32]. Fisher's LSD test for the two-way interaction Noise by Sex showed that females showed a shorter response

Table 2 Mean Response Time in Milliseconds for Correctly Identified Verbal and Non-Verbal Tokens Presented to the Left and Right Ear under the No Noise and the Contralateral Condition Separate for Male and Female Participants.

			Males (n=10)		Females (n=10)	
Noise condition	Ear of presentation	Type of Stimulus	Mean	Sd	Mean	Sd
No Noise	Left Ear	Non Verbal	990,3	124,4	1000,5	112,6
		Verbal	1019,9	124,0	980,2	89,8
	Rigth Ear	Non Verbal	972,7	125,1	968,5	110,1
		Verbal	1031,9	166,6	1006,5	84,8
Contralateral Noise	Left Ear	Non Verbal	1015,3	180,6	931,2	127,0
		Verbal	1056,0	135,7	976,5	109,2
	Right Ear	Non Verbal	937,2	125,0	932,1	141,7
		Verbal	1064,0	135,3	972,6	109,6

time during the contra lateral noise exposure. We did not find such a tendency of males (see Figure 4).

Follow-up of the significant Ear by Stimuli interaction effect with *Fisher's LSD* test for post-hoc comparisons showed a longer response time to verbal stimuli compared to nonverbal stimuli when they were presented to the right ear, but no stimulus difference was observed for stimuli presented to the left ear. Similarly, the four-way-interaction of Noise by Stimuli by Ear by Sex was close to significance [$F_{(1,16)} = 4.17$, $p = .056$, $\eta^2 =.18$], as male participants yielded a marked decrease in the response time to the nonverbal stimuli presented to the right ear that was not seen among for the female participants (See Figure 4).

Covariance analysis.

Because MOCR-induced inhibition of the CEOAE was hypothesized to be related to perception in noise skills, an analysis of covariance (ANCOVA) was conducted to control for the effect of the MOCR on the listening performance in noise experiment. The magnitude of the CEOAE inhibition scores for both left and right ear were entered as covariates in a full factorial design. The main effect of stimulus type appeared significant when left ear CEOAE MOCR was controlled for in this way [$F_{(1,12)} = 6.77$ $p = .023$, $\eta^2 = .36$], with overall longer response times for verbal compared to nonverbal stimuli. When controlling for the right ear MOCR of the CEOAER, the effect was no longer significant [$F_{(1,12)} = 2.51$, $p = .06$, $\eta^2 = .20$]. However, when both inhibition scores were controlled for at the same time, the F-quotient increased but did not reach significance [$F_{(1,12)} = 3.73$, $p = .077$, $\eta^2 = .24$].

The significance of the noise by stimulus interaction effect disappeared when the covariates were controlled for, but the noise-by-sex interaction effect remained significant and *increased* when the effect of the CEOAE inhibition was controlled [$F_{(1,12)} = 9.47$, $p < .001$, $\eta^2 = .37$]. Because the F-quotient increased by the removal of the effect of the covariate (amount of inhibition), it indicates that the covariate was related to the variance of the error term, and thus removed measurement error and increased the power of the analysis (see Miller & Chapman, 2001 for a discussion of this). Similarly, the F-value for the four-way Noise by Ear by Stimuli by Sex interaction rose to 6.84 and was statistically significant (p= .018, $\eta^2 = .30$) when the CEOAE inhibition covariates were for right and left ear were used. Post hoc testing with Fisher's LSD test on this four-way interaction showed a significant difference in response time between nonverbal and verbal stimuli when they were presented in the *right ear* of the males with or without noise (p<.01). Female participants did not show clear differences (p = .06 and .07, respectively), but showed a significant reduction in response time when nonverbal stimuli were presented in the *left ear* with contra lateral noise (p< .01). In comparison, males under the corresponding constraint showed a tendency to *longer response time* (p= .22) for nonverbal stimuli.

The four-way interaction indicates an overall tendency for longer processing times for the *nonverbal stimuli* by female participants than males (see Figure 4). *Verbal stimuli* in noise, however, appears to be processed equally fast by females and by males. Male participants use more time to process verbal stimuli with simultaneous contralateral noise, and a little less time on nonverbal stimuli, compared to the response time shown without noise. Female participants, however, show a propensity to faster response times for both the nonverbal and verbal stimuli in this context, indicating better perception of the stimuli in noise. Removal of the additional variance caused by individual differences in inhibition of the CEOAEs yielded less experimental noise and increased the power of the analyses to reveal the systematic relationship between sex and auditory performance during noise exposure.

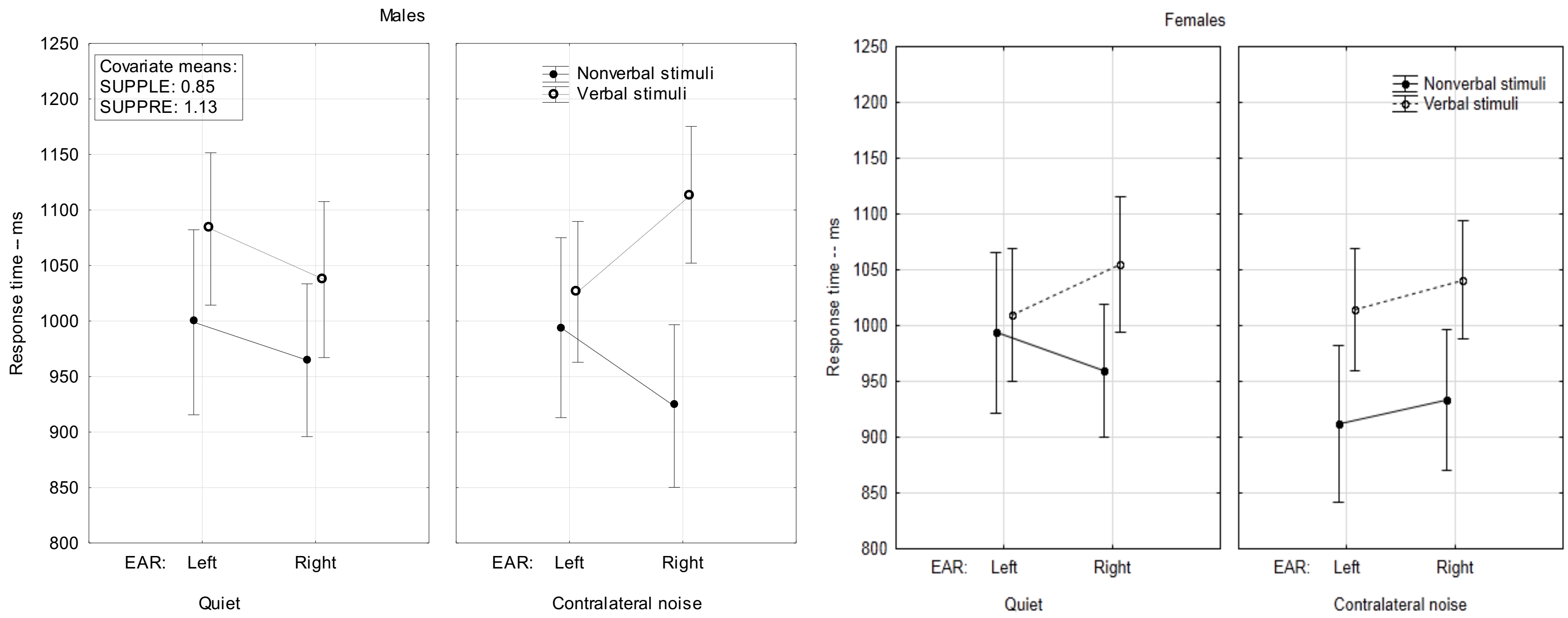

Figure 4.*The The Mean Response Times to the Verbal and Nonverbal Stimuli in Quiet and with Contralateral Noise, Separate for Left and Right Ear, Verbal and Non-Verbal Stimuli. The Response Times for Males are in the Left Hand Panel, and for Female Participants in the Right Hand Pane. The Means are adjusted According to the Control for the Effect of CEOAE Inhibition as a Covariate. The Small Bars represents +/- 1 SE*

The correlation analyses

Pearson's product moment correlation analysis between CEOAE inhibition and noise experiment showed few significant correlations (*p*< .05), but several of the pairwise correlation coefficients are in the range of .20-.40 (see Table 3). However, when conducting separate correlation analyses for male and female participants, the males yielded large correlations between laterality index of the otoacoustic emissions and response time to verbal tasks (rs > .67, p < .005), that was not found for the females (all rs < .41, n.s.).

It may seem as though CEOAE inhibition in the left ear has a relationship with nonverbal stimuli, and also the right ear CEOAE inhibition has a relationship with verbal stimuli. However, when conducting separate analyses for male and female participants, the females yielded a magnitude of the correlation that did not reach significance, although following Cohen's (1992) arguments, that r > .30 represents a medium effect size, one could infer a noteworthy relationship between CEOAE inhibition and auditory perception, in spite of the small samples used in the present study.

Table 3 Pearson's Product-Moment Correlation Coefficients between Response Time to Verbal and Nonverbal Stimuli Delivered to the Left or Right Ear with No Noise or Contra Lateral Noise, the Laterality Score for the TEOAE, and the Inhibition of the CEOAE for Left and Right Ear. The Upper Part of the Table Shows the Correlations for All Subjects, the Middle Part for Male Participants Only, and the Lower Part for Female Participants Only.

	Noise condition	Stimuli	Ear	OAE LI	CEOAE inhibition left ear	CEOAE inhibition right ear
All (N=20)	No Noise	Non verbal	Left	.02	-.25	-.11
			Right	.11	-.30†	-.16
		Verbal	Left	-.47*	-.21	-.37†
			Right	-.39†	-.21	-.27
	Contra lateral noise	Non verbal	Left	.04	-.32†	-.18
			Right	.03	-.28	-.20
		Verbal	Left	-.39†	-.27	-.44†
			Right	-.34†	-.02	-.36†
Males (n=10)	No Noise	Non verbal	Left	-.06	-.02	-.11
			Right	.03	-.04	-.06
		Verbal	Left	-.72*	.29	-.12
			Right	-.56*	.37	.04
	Contra lateral noise	Non verbal	Left	-.14	.05	-.09
			Right	-.07	.07	.04
		Verbal	Left	-.68*	.34	-.02
			Right	-.68*	.40†	.06
Females (n=10)	No Noise	Non verbal	Left	.18	-.15	-.14
			Right	-.25	-.26	-.20
		Verbal	Left	-.25	.50	.45†
			Right	-.13	.43†	.43†
	Contra lateral noise	Non verbal	Left	-.24	-.03	-.04
			Right	.16	.01	.04
		Verbal	Left	-.30	.25	.08
			Right	-.24	.31	.24

** = significant correlations, p < .05, † = non-significant, intermediate effects, r > .30*

In addition, significant correlations were also seen for the emissions and the dichotic listening performance (Table 1). Over all, positive correlations for the right ear performance of the right ear reports during the forced right task and the emissions from the right ear (rs > .52, $p < .05$) and for the forced left task (rs > .48, $p < .05$) were found. However, for the female participants alone, the correlations were stronger for the non-forced task (rs > .68, $p < .05$) compared to the forced attention tasks (all rs < .46, n. s.), but for the male participants alone, the correlations were stronger for the forced right task (rs > .73, $p < .05$). Also, the correlations were found to be stronger in the mid frequency bands for the females (e. g. 1.0 kHz 1.4 kHz rs > .64, $p < .05$) but stronger in the higher frequency bands for males (e.g. 2.8 kHz, rs > .67, $p < .05$).

Discussion

The results from this study supports previous studies (see Velenovsky & Glattke, 2007) that have reported sex differences in the OAE and OAE MOCR, as the female participants showed significantly larger CEOAE and also larger CEOAE inhibition effects than males. We also found larger inhibition effects in the lower frequency bands than in the higher frequency bands that were also expected (Morand et al., 2000).

However, the quite robust frequency dependent sex differences that were seen for both CEOAE in quiet and with contralateral noise were surprising and have not been reported in the literature earlier. This sex by noise interaction was robust ($\eta^2 = .41$), and suggests that a genuine sex difference in hearing. Although the three way sex by noise by frequency band interaction was not significant, inspection of the mean values (see Figure 1) suggests that female participants show similar CEOAE amplitudes across all frequency bands that were assessed and with approximately the same magnitude of the MOCR across frequency bands, but the male participants showed CEOAE with a smaller amplitude for the low and high frequency bands, and with visible effects of the MOCR only for the lower frequencies.

The interaction of sex and noise yielded a significant effect for response time to auditory stimuli, as the difference in response time with and without noise was only observed among the females, who showed faster response time when the noise was presented contra laterally. Males, however, showed a tendency to longer reaction time, a finding that was surprising, but still support a notion of sex differences in processing of auditory stimuli. Therefore, we only found partial support for the hypothesis that contralateral noise causes faster responses to auditory stimuli, due to a “release from masking” effect. The hypothesis that a contralateral noise effect leads to faster auditory response time seems to be supported by the females’ performance, but not the males’.

There was also a significant interaction effect between the ear and stimulus type, as nonverbal stimuli presented to the right ear yielded a faster response than the verbal stimuli. This difference can probably be explained by the differences in stimulus salience, including their longer duration, as nonverbal stimuli were slightly easier to identify in the noise conditions compared to the CV syllables. Figure 1 shows a slight tendency toward right ear benefit for processing of nonverbal stimuli, and a left ear benefit for verbal stimuli, which is contrary to what was expected.

Other studies (e.g. de Boer & Thornton, 2007; Garinis, Glattke, et al., 2011; S. B. Smith & Cone, 2015) have also found effects of directed attention on CEOAE, and as such biased attention may also be a source of variance involved in the present findings. Early theoretical models for the lateralized perceptual effects of dichotic and dichoptic presentation

(Kinsbourne, 1983) also included notions of how activation of a specialized cerebral hemisphere caused a bias of attention to the contralateral perceptual field. However, as specific control for attention was not applied in the present experimental tests, we cannot rule out attention as an alternate explanation. This is a limitation of the study, and a replication of the study should probably also include procedures for active control of attention fluctuations.

The results of the correlation analyses show that ear differences for the MOCR, that is, the laterality, can explain a portion of the variance in response time for auditory processing. The effect is strongest for processing of verbal stimuli in the contra lateral noise condition ($r > .39$). Furthermore, MOCR magnitude yields a relationship with auditory processing through shared variance with both the response time and noise condition with contralateral noise. These effects are more specific, as the MOCR magnitude in right ear correlates with response to verbal stimuli ($r > .36$) and the MOCR in the left ear correlates with response time to nonverbal stimuli ($r > .30$), although these coefficients did not reached the level for statistical significance. These are, however, medium effect sizes (Cohen, 1992) representing 10% shared variance.

These findings suggest a functional relationship between the MOCR in the right ear and perception of verbal stimuli, and between the MOCR in the left ear and perception of nonverbal stimuli, which is in line with our main analysis. The results support classic studies of laterality (Kimura, 1967; Sininger & Cone-Wesson, 2004) wherein verbal stimuli presented to the right ear are processed more quickly than in the left ear due to the more efficient contralateral pathway to the left hemisphere language centre. Similarly, non-verbal stimuli with high spectral complexity are processed more efficiently when presented to the left ear with its stronger contralateral connection to the right hemisphere. Such laterality differences in CEOAEs are present at birth (Sininger & Cone-Wesson, 2004). The present data further support earlier studies that have suggested that the MOC effect mediates the ability to understand auditory stimuli in a steady stream of noise (Anderson, Parbery-Clark, Yi, & Kraus, 2011; Bright, 2007; Giraud, Garnier, et al., 1997; Kim, Frisina, & Frisina, 2006).

The findings suggest that females and males respond differently to noise, and we assume that the MOCR, may, in part, explain this sex difference. Females tend to show improved perception in contralateral noise, while it seems that the noise has a negative influence on males' perception of auditory stimuli. Faster response times in noise correlated with an increased inhibition in the females, who generally showed larger MOCR than males.

Studies with experimental animals suggest that a stronger OAE in females than in males is a fundamental pattern of mammals in general, as similar tendencies have been reported in rhesus monkeys (McFadden, Pasanen, Raper, Lange, & Wallen, 2006) and sheep (McFadden, Pasanen, Valero, Roberts, & Lee, 2009). It is important to further consider whether sex differences are due to anatomical differences in the ear canal or the middle ear, which leads to different acoustical properties, or whether females and males shows more general differences in auditory processing.

These findings may have some relevance to the understanding of auditory processing disorders. There are a number of studies that document that understanding speech in noise is particularly challenging for those with auditory processing disability (for review see Moore et al, 2013). Abnormalities in lateralization are also documented, that is, there are those who demonstrate little or no right ear advantage for speech (Iliadou, Kaprinis, Kandylis, & St Kaprinis, 2010; Schmithorst, Farah, & Keith, 2013). Similarly, the MOCR is atypical in those with auditory processing issues, and, in fact, may demonstrate deviation from the typical lateralized effects (Garinis, Glattke, & Cone-Wesson, 2008; Muchnik et al., 2004; Sanches & Carvallo, 2006; Veuillet, Magnan, Ecalle, Thai-Van, & Collet, 2007). Thus, it may be that the MOCR strength and the ear effects offer a means for understanding lower brainstem factors that underlay perceptual difficulties in speech-in-noise understanding. There are sex-differences in auditory perception (C. P. Brown, Fitch, & Tallal, 1999) and processing (Andoh & Zatorre, 2011) and studies in experimental animals point to the differential effects of estrogen in the central auditory system of female and males (Charitidi & Canlon, 2010; Pinaud & Tremere, 2012).

Conclusion

The results of this study showed that the MOCR mediated inhibition of CEOAEs can explain the some aspects of auditory perception in noise. The present findings support earlier research that shows a functional lateralization in the peripheral auditory system (Sininger & Cone-Wesson, 2004) where the crossing auditory nerve path seems to be more robust than the ipsilateral (Kimura, 1967). We also found that females and males apply different perceptual processes when stimuli are presented simultaneously with broadband noise. Females showed a larger MOCR than males, and there is speculation as to how the MOCR can more fully account for the different capabilities to discriminate auditory signals in noise.

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