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Interaural attention modulates outer hair cell function

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Abstract

Mounting evidence suggests that auditory attention tasks may modulate the sensitivity of the cochlea by way of the corticofugal and the medial olivocochlear (MOC) efferent pathways. Here, we studied the extent to which a separate efferent tract, the “uncrossed” MOC, which functionally connects the two ears, mediates inter-aural selective attention. We compared distortion product otoacoustic emissions (DPOAEs) in one ear to binaurally-presented primaries, using an intermodal target detection task in which participants were instructed to report the occurrence of brief target events (visual changes, tones). Three tasks were compared under identical physical stimulation: (1) report brief tones in the ear in which DPOAE responses were recorded; (2) report brief tones presented to the contralateral, non-recorded ear; (3) report brief phase shifts of a visual grating at fixation. Effects of attention were observed as parallel shifts in overall DPOAE contour level, with DPOAEs relatively higher in overall level when subjects ignored the auditory stimuli and attended to the visual stimulus, compared with both of the auditory-attending conditions. Importantly, DPOAE levels were statistically lowest when attention was directed to the ipsilateral ear in which the DPOAE recordings were made. These data corroborate notions that top-down mechanisms, via the corticofugal and medial efferent pathways, mediate cochlear responses during intermodal attention. New findings show attending to one ear can significantly alter the physiological response of the contralateral, unattended ear, likely through the uncrossed-medial olivocochlear efferent fibers connecting the two ears.

Keywords

corticofugal pathways; medial olivocochlear efferents; interaural selective auditory attention; distortion product otoacoustic emission; DPOAE; human

Introduction

A growing literature suggests that selective attention tasks produce alterations in peripheral auditory system function (Puel *et al.*, 1988; Meric & Collet, 1992, 1994; Giard *et al.*, 1994;

Maison *et al.*, 2001; Delano *et al.*, 2007; Srinivasan *et al.*, 2012). For instance, Delano and colleagues (2007) measured both the auditory nerve compound action potential (CAP) and cochlear microphonic (CM) response to auditory signals in chinchillas during visual and auditory tasks. Paralleling earlier work in cats (Oatman, 1971), Delano *et al.* (2007) reported that CAPs recorded during visual discrimination tasks were smaller than CAPs recorded during auditory discrimination. Importantly, they also found that the CM response increased during the visual task, indicating a descending, efferent role in modulating outer hair cell (OHC) function.

Work employing otoacoustic emissions (OAEs) has also described systematic changes in cochlear function during selective attention (Meric & Collet 1992; Giard *et al.* 1994; Maison *et al.* 2001; Smith *et al.*, 2012; Srinivasan *et al.*, 2012). OAEs, generated by the active mechanical response of OHCs to sound, can be measured in the external ear canal of human listeners (Wilson, 1980; Probst *et al.*, 1991; Yates *et al.*, 1992). In many of these studies, DPOAEs were *decreased* when recorded to *attended* auditory primaries, consistent with the tuning characteristics of the medial olivocochlear (MOC) tracts (Murugasu & Russell, 1996; Brown, 1989; Delano *et al.*, 2007; Srinivasan *et al.*, 2012). In OAE studies of attention, subjects often attend to primary tones, yet DPOAEs are measured at tonotopic locations remote from the attended primaries (Shera & Guinan, 1999). Thus, given the suppressive nature of MOC activity (Robertson, 2009; Guinan, 2010), MOC-mediated effects may result in suppression of *ignored* frequencies, in this case, the DPOAE (Smith *et al.*, 2012; Srinivasan *et al.*, 2012). Supporting this notion, detection accuracy of unexpected tonal frequencies is decreased with tonotopic distance from the expected frequency (cf., Dai *et al.*, 1991; Strickland & Viemeister, 1995).

Corticofugal pathways project from auditory cortex down to the olivary complex within the brainstem, then reach out to the cochlea via the MOC tracts, where they terminate on OHCs (Warr *et al.*, 1986; Schofield, 2010). Their functional connectivity is demonstrated by altered cochlear responding following electrical stimulation of the cortex in experimental animals (Xiao & Suga, 2002; Suga, 2008; Liu *et al.*, 2010) and humans (Perrot *et al.*, 2006). In addition to corticofugal/MOC tracts, the two ears are functionally connected by uncrossed-medial olivocochlear efferent fibers (Warr *et al.*, 1986); acoustic or electrical stimulation of one ear suppresses responding in the contralateral cochlea (Warren & Guinan, 1989; Smith *et al.*, 1994; Perry *et al.*, 1999; Bassim *et al.*, 2003). The functional role of this interaural, efferent innervation system in selective attention is not currently known, although recent data (de Boer & Thornton, 2007) suggest that it decreases the effects of noise on signal detection during attention. The present study examined the hypothesis that shifting attention from one ear to the other produces systematic alterations in monaural cochlear function, reflective of involvement of the uncrossed MOC.

Methods

The instrumentation and experimental procedures employed in this study were described in a previous report, and are described in more detail there (Srinivasan *et al.*, 2012).

Participants

Ten college-aged students (18 – 20 years old, seven females) participated in this experiment. Prior to testing, a brief history was taken from each participant to document ear-related complaints, such as current ear congestion or infection, history of ear infections, ear surgery, noise exposure, music player and headphone use and ototoxic and chronic medication use.

All experiments were approved by the Institutional Review Board of the University of Florida. The experiments were undertaken with the understanding and written consent of each participant. This study conforms with the 2013 World Medical Association Declaration of Helsinki.

Instrumentation and stimulus parameters

The equipment, auditory stimuli and DPOAE recording and analysis procedures have been described in previous reports (Srinivasan *et al.*, 2012). Briefly, two digitally-generated primary tones (RX6 and RP2.1 DSP processors, Tucker-Davis Technologies, Gainesville, FL, USA) were fed individually to two transducers in each ear (Etymotic Research, Elk Grove Village, IL, USA). The primaries and the otoacoustic emissions were measured in the ear canal with a low-noise microphone probe (ER 10B+, Etymotic Research), sampled continuously at a rate of 48.83 kHz, digitized (Tucker-Davis Technologies), and stored to the hard drive.

Auditory stimuli

The primary tones f_1 and f_2 were presented with a frequency ratio $f_2/f_1 = 1.21$ and f_1 level = 70 dB SPL and f_2 level = 65 dB SPL. A DPgram, assessing the sensitivity of the ear across a range of frequencies, was constructed by varying the f_2 frequency in a 20-step geometric progression from 1.2 to 10.8 kHz, and the frequency producing the strongest DPOAE level in either ear for each subject was selected as the recorded (ipsilateral) ear during the experiment. The primary tones, though chosen to generate the largest DPOAE in the recorded ear, were presented in binaurally at all times in order to produce the largest measurable response in the ear selected for study (Lieberman *et al.*, 1996; Bassim *et al.*, 2003). Responses from the contralateral ear, though collected, were not further analyzed.

The primary tones presented to each ear were either 1 or 2 s in duration (~20% 1 s and ~80% 2 s), presented in a randomized manner with an inter-trial interval of 2 s. The onset of the tones to both ears was simultaneous, regardless of duration. Using long – duration tones, as opposed to transient or click stimuli, to measure DPOAEs offers the advantage of characterizing both the presence of MOC activity as well as its onset time course (cf., Lieberman *et al.*, 1996; Kim *et al.*, 2001; Bassim *et al.*, 2003). The rise/fall times of all stimuli were zero, with the primaries beginning at 0° of phase in order to reduce the effects of frequency splatter. This splatter was further minimized by measuring the DPOAE amplitude at the $2f_1$ - f_2 frequency peak, discarding the first ~1 ms, with a bin width of 11.92 Hz.

At the start of each session, the eartip transducers/microphone assembly was positioned within the external ear canal and the acoustic system output was calibrated. Calibrations

were repeated throughout the session to detect the emergence of small changes in probe placement or orientation. During each session, primary tone and DPOAE levels were plotted on screen on a stimulus-by-stimulus basis and any sudden, or systematic change in signal levels, usually indicating a displacement of the probe/microphone system in the ear canal, resulted in the session being interrupted. In these situations, the earphones were re-positioned and the system was recalibrated.

Visual stimuli

All visual stimuli were presented on a flat-panel monitor, situated 72" directly in front of the participant. During each trial, after presentation of a fixation cross, Gabor patches, oriented 45° to the right of vertical, were presented in the center of the screen. Each Gabor patch was composed of seven alternating black/white sinusoidal bars whose greatest contrast (99.8% Michelson) was at the center of the stimulus, with a Gaussian decline to the edges. The Gabor patch subtended a visual angle of 2.18° with 3.21 cycles per degree. After a 1 or 2-s delay (presented randomly in a session, ~20% 1 s and ~80% 2 s), the patch was phase shifted by 180°. The visual stimulus was presented for a total of 3 s in each trial with an inter-stimulus interval of approximately 2 s. During the inter-stimulus interval, a fixation cross was present occupying 0.8° of visual angle.

A miniature video camera, connected to a monitor outside of the sound chamber, permitted monitoring of the participant's behavior during the test session. The onset of visual stimuli and auditory stimuli presented in each trial were offset, with the visual stimulus onset delayed with respect to the auditory stimulus by a random interval ranging between 500 and 1000 ms from the onset of the auditory stimulus. The random delay interval was introduced to prevent participants' usage of the other modality, respectively, to identify short-duration targets. Post-experimental assessment of the strategy adopted by the participants suggested that they focused solely on the to-be-attended modality to complete the task.

Behavioral Task

Participants were instructed to press a response key when a target event was detected. Three different attention conditions were tested (Figure 1). In the attend-visual condition, participants ignored all (binaural) auditory stimuli and were instructed to respond to the short latency phase change in the (visual) Gabor patch. In the first auditory-attending condition (attend-ipsilateral), participants were instructed to attend to the ear in which the DPOAEs were recorded and to report a short-duration tone, while ignoring contralateral auditory stimuli and the visual Gabor patch. In the second auditory-attending condition (attend-contralateral), participants were instructed to report detection of a short-duration tone presented to the contralateral ear, while ignoring the auditory stimulus in the DPOAE-recorded ear and the Gabor patch. Each attention condition was indicated by text on the screen before each session started. An arrow presented on the screen prior to each trial served to instruct the participants to attend to the left or the right ear. In attend-visual conditions, text instructed participants to attend to the visual stimuli.

DPOAE analysis

The microphone signals were divided and a real-time Fast Fourier Transform was performed by a second computer during each trial to monitor the levels of primary signals, as well as to monitor for the presence of the 2f1-f2 DPOAE. During data analysis, a two-component exponential was fitted to the DPOAE contours (Sigma Plot; Systat Software, San Jose, CA) to facilitate calculation of the magnitude of adaptation, as well as the adaptation onset time constant (cf., Kim *et al.*, 2001). A participant's data were included in the overall analysis only if the observed rapid adaptation was larger than the measured variance in the adaptation contour; using this criterion gave confidence that MOC activity, necessary for any attentional effects, could be observed in that participant's DPOAE response. Absolute DPOAE levels across attention conditions were estimated by averaging the data points in each trace from 750 ms to 1000 ms.

Statistical analysis

For DPOAE levels and behavioral accuracy, the results obtained from each participant under each of the three attention conditions were compared statistically using repeated measures analysis of variance (ANOVA) with a within-subjects factor of Condition (attend-visual, attend-ipsilateral, attend-contralateral). A significant effect was followed by contrast analysis, including linear versus quadratic contrasts among the three means.

Experimental procedure

All experiments were conducted inside of an IAC (Industrial Acoustics Corporation, Bronx, NY, USA) sound-attenuating chamber. After initial screening, participants were seated in comfortable reclining chair within the sound booth, detailed instructions were provided, eartip recording probes were inserted in both ears and the calibrations performed. DPOAE responses were recorded and saved to disk, and the responses from the ear with the selected DPOAE (ipsilateral ear), were averaged across subjects. Trials with variations in the primary levels and/or DPOAE responses (greater than the magnitude of rapid adaptation) were discarded before calculating averages. At least eight sessions under each attention condition (see above) were conducted, with 16 trials in each session.

Auditory stimuli of 1- (short) or 2-s (long) duration were pseudo-randomly presented binaurally in each session with ~20% of the trials of the short duration. Visual stimuli were presented simultaneously on the screen in front of the participant, starting with a short pseudo-randomized delay of 500-1000 ms after auditory stimuli onset. The visual stimuli changed phase either after 1 s (short) or 2 s (long) after onset and stayed on the screen for a total of 3 s before being replaced by a fixation cross. Short visual stimuli were presented in ~20% of the trials in a pseudo-randomized fashion in a session (the pseudo-random order not coupled with that of the auditory stimuli).

Results

Behavioral results

The percentage of mean hits (responding to the short-duration primary tones) was 93.08 for the ipsilateral ear attention condition, 86.54 for the contralateral ear attention condition and

84.54 for the visual attention condition. False alarms (responding to the long-duration primary tones) were 1.17% for the ipsilateral ear attention condition, 1.70% for the contralateral attention condition and 9.63% for the visual attention condition (reporting detection of the short-latency phase change in the Gabor patch). ANOVA indicated that there was no statistically significant difference between the mean hit percentages across the attend ipsilateral, attend contralateral and attend visual conditions, $F(2,16) = 0.665$, $p = 0.528$. False alarm percentages, however, were significantly different across the three conditions resulting in a main effect $F(2,16) = 8.699$, $p = 0.003$. A linear contrast $F(1,8) = 12.074$, $p = 0.008$ modeled false alarms condition differences with attend-ipsilateral < attend-contralateral < attend-visual.

DPOAE results

Figure 2 shows the individual DPOAE contours for 10 listeners under three attending conditions; while attending to the visual Gabor patches and ignoring all auditory tones in both ears (attend visual; solid blue line), while attending to the DPOAE-eliciting tones in the recorded ear and ignoring the contralateral tones and visual Gabor patch (attend ipsilateral; solid red line), and while attending to the contralateral tones and ignoring the recorded ear tones and visual Gabor patches (attend contralateral; dashed-red line). While considerable inter-subject variability is evident, in general, changes in attending conditions produced parallel shifts in the absolute level of the recorded DPOAE adaptation contours. The absolute onset level of DPOAEs while participants attended to the visual distractor, and ignored all auditory tones (attend visual), was relatively highest in 9 of 10 participants. Figure 3 shows the difference from the DPOAE onset level (attend visual) in the attend contralateral and attend ipsilateral conditions. When listeners ignored the visual distractor and attended to the tones presented in the DPOAE-recorded ear (attend ipsilateral), DPOAE onset levels were relatively lower in overall level in 8 of 10 participants, compared with when they attended to the tones presented in the contralateral ear (attended contralateral).

Figure 4 shows the average DPOAE adaptation contours measured for the 10 listeners in each of three attending conditions. Consistent with previous results, mean adaptation contours show that DPOAEs recorded during the attend visual condition (solid blue line) were relatively highest in overall level compared with DPOAEs recorded during both auditory attending conditions (attend ipsilateral; solid red and attend contralateral; dashed-red lines). The results also show that DPOAEs were lowest in overall level when listeners responded to target stimuli presented to the ipsilateral, recorded ear (solid red line). Comparing the two auditory-attending conditions, on average, the amplitude of the DPOAE recorded while participants attended to the tones presented in the contralateral ear was statistically higher in overall level, approximately 0.08 dB, than the amplitude of DPOAEs recorded while attending to the tones presented in the ipsilateral, recorded ear. The data also show that attending to the visual Gabor patches (attend visual), while ignoring auditory stimuli presented in both ears, resulted in the highest overall DPOAE levels; the mean DPOAE amplitude recorded while listeners ignored all tones presented in both ears, and attended to the visual distractor was 0.1641 dB higher than the DPOAE amplitude when subjects attended to the ipsilateral, recorded ear and 0.08 dB higher than when listeners attended to the contralateral, non-recorded ear. ANOVA indicated that this linear increase of

DPOAE means from the lowest levels during attend-ipsilateral to the highest levels during attend-visual trials was statistically significant, resulting in a main effect of condition, $F(2,18) = 6.4$, $p < 0.01$. A linear contrast $F(1,9) = 11.3$, $p < 0.01$, modeling condition differences as attend-ipsilateral < attend-contralateral < attend-visual, supported the hypothesis that DPOAE means increase as attention is directed away from the recorded ear.

Discussion

Attending to a stimulus typically results in a relatively larger signal in the corresponding sensory cortical areas, compared with when the same stimulus is ignored (c.f., Woldorff et al., 1987; Johnson and Zatorre, 2005; Kauramäki et al., 2007; Saupe et al., 2009). The present results add to a growing body of work suggesting that attention tasks affect auditory function at lower levels, including the sensory periphery. Using a binaural intermodal selective attention task, we observed attention-dependent, parallel shifts in absolute DPOAE levels recorded during different intra- and intermodal attending conditions. Consistent with previous results (Smith *et al.*, 2012; Srinivasan *et al.*, 2012), DPOAEs recorded while listeners attended to a visual distractor (attend visual), and ignored the auditory tones, were relatively *higher* in overall level compared with when participants attended to the same auditory stimuli and ignored the visual Gabor patches. These data, combined with previous studies (Delano *et al.*, 2007; Smith *et al.*, 2012; Srinivasan *et al.*, 2012), demonstrate that the effects of attention are evident as modifications in responding at the most peripheral aspects of the auditory system, within the cochlea. These findings also support the notion that shifts in the focus of attention, through the descending, corticofugal and medial olivocochlear efferent pathway, produce a systematic alteration in the operating set point of the outer hair cell active mechanical process within the cochlea.

The neural mechanisms underlying the novel *interaural* attention effects reported here may, however, be more complex. In this study we show significant changes in overall DPOAE levels when subjects shifted the focus of attention from the ipsilateral, DPOAE recorded ear to the contralateral ear; attending to the ipsilateral ear results in DPOAEs that are relatively lower in overall amplitude, compared with DPOAEs recorded in the same ear while participants attended to the same primary tones presented in the contralateral ear. Because DPOAEs are generated by the mechanical response of OHCs, attention must be acting via an MOC-mediated mechanism, yet there are at least two different MOC pathways by which this effect could be produced. The first mechanism is via the corticofugal MOC pathway, descending from the auditory cortex, through the MOC fibers innervating the OHCs within the ipsilateral, recorded ear. Recently, León *et al.* (2012) have demonstrated alterations in cochlear responding following pharmacologic deactivation of the auditory cortex in chinchillas, which are suggestive of a descending, tonic influence over OHC function. A similar effect was demonstrated in humans who had undergone resection of the temporal superior gyrus to reduce epileptic seizures (Khalfa *et al.*, 2001). Using this pathway, descending attentional influences could act on each ear independently, depending on which ear was being attended to. This mechanism may suppress activity in each cochlea without an *interaural* component, and has been assumed in previous intermodal work where cochlear responding was compared during visual or monaural auditory attending tasks (Delano *et al.*, 2007; Smith *et al.*, 2012; Srinivasan *et al.*, 2012). This explanation, however, would require

that the observed differences in overall DPOAE level when contralateral- and ipsilateral-attended DPOAEs are compared, that each respective auditory attending condition would stimulate, for the same auditory stimulus, the same crossed-MOC population in a different manner, perhaps as a difference in MOC discharge rate.

A second MOC mechanism involves the uncrossed MOC fibers that functionally connect the two ears. The terms crossed and uncrossed refer to whether or not the MOC fibers themselves cross the midline to innervate the OHCs; (Warr *et al.*, 1986; Guinan & Gifford, 1988). It has long been known that acoustic or electrical activation of one ear, through the uncrossed MOC, will suppress the activity of the contralateral ear (cf., Robertson, 2009; Guinan, 2006). The current findings suggest that, when alternating attention between ears, this interaural pathway may function to further suppress processing of non-attended frequencies in the attended ear when suppression through crossed MOC is released on the other (non-attended) ear. This suggestion is also supported by the work of de Boer & Thornton (2007) who demonstrated that attending to one ear results in a diminution of contralateral noise induced suppression, mediated by the uncrossed MOC, of click-evoked otoacoustic emissions in the attended ear.

An additional line of evidence arguing for a role of the uncrossed MOC in interaural attention comes from a comparison of the relative amplitude of DPOAEs while participants attended to the visual stimulus (i.e., they ignored all auditory stimuli) with DPOAE amplitudes when they attended to either the ipsilateral or the contralateral ears alone. It has long been known that the magnitude of efferent suppression of OHC activity is dependent on the relative number of MOC fibers activated (Warr *et al.*, 1986; Liberman & Brown, 1986; Brown, 1989). While the ratio of crossed to uncrossed fibers is unknown in humans, in most small mammals approximately two-thirds of MOC fibers synapsing on OHCs are crossed-MOC fibers, which respond to ipsilateral sound (and corticofugal activation), with the remaining one-third being uncrossed-MOC fibers that are responsive to stimulation in the contralateral ear. Gifford and Guinan (1987) conducted a series of studies investigating the action of the two MOC subgroups on cochlear potentials in the cat. In that study, the crossed and uncrossed MOC pathways in the brainstem were individually stimulated, and effects on cochlear potentials measured. They noted a relatively larger effect on cochlear potentials when the crossed MOC was selectively stimulated, compared with when the uncrossed tract alone was activated. Gifford and Guinan argued that the magnitude of the MOC effect on the cochlea was proportional to the number of fibers within each MOC subgroup. Numerous subsequent studies have reported mechanistically similar effects in both non-human animals and in humans (cf., Liberman *et al.*, 1996; Bassim *et al.*, 2003), where larger effects are reported when both crossed and uncrossed subpopulations are stimulated, compared with either subgroup alone. Likewise, the present observations may be explained by the same notion; with each attentional condition activating a different efferent sub-group (or groups) that, owing to the different number of fibers contained in each, produces different magnitudes of suppression. For example, when participants were instructed to ignore all auditory stimuli, possibly less activating the relatively larger crossed MOC tract via the corticofugal pathway, relatively larger DPOAE were observed, while attending to the contralateral or ipsilateral ear result in relatively smaller DPOAEs because

only the crossed and uncrossed tracts differ in their level of suppression of the respective other ear. Further work is required to confirm this suggestion.

Additionally, it should be mentioned that an additional, lateral olivocochlear (LOC) tract descends from the lateral olivary complex in the brainstem to post-synaptically innervate type I afferents beneath inner hair cells. Recent work has shown that these LOC fibers may function to balance the acoustic input between the ears, possibly playing a role in sound localization (Irving *et al.*, 2011). Because LOC fibers do not innervate, or directly influence OHC function, they cannot play a functional role in modulating the DPOAE measures employed here.

In earlier work, Woldorff and colleagues (1987) used a dichotic listening to compare cortical responses when participants attended to an auditory stimulus with when they ignored it. Using this approach, they showed an increase in middle latency (P20-50) and long latency (N1P2) responses with shifts in the locus of attention from one ear to the other. Broad consensus in current human electrophysiology has adopted the view that the very early auditory (brainstem) potentials are not reliably affected by attention (e.g., Picton, 2010). Yet, the present data, we believe, show that attention effects extend to the periphery, when using a balanced set of experimental conditions challenging attention over extended periods of time; the identical auditory stimuli were presented to both ears in all attending conditions, and the only differences are in the focus of attention. Earlier studies by Giard *et al.* (1994) and Michie *et al.* (1996) recorded and compared evoked otoacoustic emissions (EOAEs) while manipulating selective auditory attention. Giard and colleagues (1994) presented dichotic stimuli with 1 kHz in one ear and 2 kHz in the opposite ear. The participants were instructed to count occasional targets in the right ear and ignore the tones in the left ear, or ignore the right ear and attend to the left ear. They reported evoked otoacoustic emissions (EOAE) as being higher for the attended tones than when they were unattended. Michie and colleagues (1996) employed a similar design in a series of six experiments, using both dichotic stimuli and stimuli presented to one ear alone. In the first five experiments, they presented two different frequency tones to one ear, without stimuli presented to the contralateral ear, and compared EOAEs while manipulating attention to either of those two frequency tones. They reported finding no effect of changes in attention in any of those conditions. In the sixth experiment, they employed binaural tones, presented at different frequencies to the two ears, in an attempt to replicate the design by Giard *et al.* (1994). In this experiment, EOAEs were compared while participants attending to one ear and ignored stimuli presented to the other ear, with when the attending conditions were reversed. Under these conditions, they observed a decrease in the amplitude of EOAEs to attended stimuli, as we report here, the opposite of effects reported by Giard *et al.* (1994). It is important to point out that neither Giard *et al.* (1994) nor Michie *et al.* (1996) presented an attentional control condition.

As with previous studies where changes in cochlear function were observed following intermodal shifts in attention (Lukas, 1980, 1981; Michie *et al.*, 1996; Delano *et al.*, 2007; Smith *et al.*, 2012; Srinivasan *et al.*, 2012), the relatively lower DPOAE amplitudes observed in the present work when listeners counted targets in the DPOAE recorded ear, compared with when they reported shifts in Gabor patch phase, may be explained as

resulting from the known properties of the MOC on OHC function. The corticofugal pathways descend from the auditory cortex and exert control over OHC and cochlear function through MOC synapses on the subnuclear regions of OHCs (cf., Warr *et al.*, 1986; Warr, 1992; Schofield, 2010). MOC fibers influence the active mechanical actions of OHCs by altering the conductance of the cell membrane and, in doing so, reduce the gain of the cochlear amplifier (cf., Guinan, 2010). The direct involvement of MOC suppression of OHCs in the attentional process can be observed as an increase in the CM potential associated with the decrease in CAPs when animals attended to a visual task (Delano *et al.*, 2007).

As with our earlier studies, we did not observe a difference across attending conditions in the time course of the rapid adaptation component of the DPOAE (Smith *et al.*, 2012; Srinivasan *et al.*, 2012). This finding is important because rapid adaptation is known to be a consequence of medial efferent action on cochlear OHCs (Liberman *et al.*, 1996). Because rapid adaptation is still evident and unchanged across attending conditions, this suggests that, at least, two different MOC functions are evident in the results - rapid adaptation, which is unaffected by attention, and optimization of the gain of OHC active mechanisms, which is under attentive influence. Consistent with previous studies (Delano *et al.*, 2007; Smith *et al.*, 2012; Srinivasan *et al.*, 2012), these observations show that descending neural systems alter peripheral auditory system physiological function – via OHC receptor mechanical sensitivity – in a manner dependent upon the attentional task at hand.

The present results, showing a *decrease* in DPOAEs when participants attend to the eliciting tones, are in agreement with previous DPOAE studies (Michie *et al.*, 1996; Smith *et al.*, 2012; Srinivasan *et al.*, 2012). As we have discussed in those previous reports, this finding is the opposite of previous results from a number of investigators employing different, electrophysiological measures of peripheral auditory function (cf., Oatman, 1971, 1976; Lukas, 1980, 1981; Delano *et al.*, 2007). It is also the opposite of the generally accepted effect observed cortically (Woldorff *et al.*, 1987; Johnson & Zatorre, 2005; Kauramäki *et al.*, 2007), which is a relative *increase* in the amplitude of attended signals. DPOAEs are produced by the nonlinear mechanical behavior of cochlear OHCs to two primary tones (Wilson, 1980; Probst *et al.*, 1991; Yates *et al.*, 1992). In the present experiment, participants are instructed to attend to the DPOAE primary tones, but the recorded 2f1-f2 DPOAE is produced at a frequency some cochlear distance below the primaries (in DPOAE studies, the recorded DPOAE frequency can not be heard by the listener) and, depending on the sharpness of MOC tuning, attending to the primaries likely results in a suppression of the DPOAE response (Greenberg & Larkin, 1968; Dai *et al.*, 1991; Strickland & Viemeister, 1995). Additional research is necessary to explain this effect. While the explanation for the decrease in DPOAEs with attention remains unclear, there are now sufficient, converging lines of evidence to confirm that the initial effects of attentional processing are evident at the level of the OHCs.

It is important to point out that, while the magnitude of observed changes in overall DPOAE levels with shifts in attention may be small, approximately 0.1 – 0.2 dB, this should not be taken as reflecting the expected magnitude of attention effects possible in real world listening conditions. The critical point from this work is that attention-induced changes in

auditory processing can be observed at the very earliest stages of auditory processing, and that these effects include an interaural component. In these experiments, rather than optimizing stimulus conditions to produce the largest overall DPOAEs in each individual, we chose to employ standardized stimulus conditions across listeners; the frequency ratio was fixed at $f_2/f_1 = 1.21$ and primary tone levels were $L_1 = 70$ dB SPL and $L_2 = 65$ dB SPL. The coincident onset of the binaural primaries was employed to most effectively elicit maximal MOC activity at the chosen frequency - which could be observed as the rapid adaptation of DPOAE level following primary tone onset - an indicator of descending control over cochlear function. The magnitude of the overall, attention-mediated suppression of cochlear responses to unattended auditory stimuli under natural listening conditions, however, is unknown. Skjönsberg *et al.* (2007) have shown that through a complex primary tone frequency and level optimization procedure, the magnitude of MOC effects on cochlear activity may be as large as 48 dB, suggesting that there exists a potential that the *cochlear response* to an ignored sound might be reduced by over 90% of the attended level.

It is clear from a growing literature, including the present work that changes in the focus of attention produce significant alterations in the cochlear sensitivity. New data, presented here, show for the first time that interaural shifts in attention produce significant changes in the sensitivity of the unattended ear. Further work is required to identify the specific neural mechanisms underlying this effect, as well as to determine the magnitude of attentional effects within the cochlea.

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Abbreviations

MOC	Medial Olivocochlear
DPOAE	Distortion Product Otoacoustic Emission
CAP	Compound Action Potential
CM	Cochlear Microphonic
OAE	Otoacoustic Emission
DPgram	Distortion Product-gram
ANOVA	Analysis Of Variance
EOAE	Evoked Otoacoustic Emission
OHC	Outer Hair Cell
LOC	Lateral Olivocochlear

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Figure 1.

Schematic of three different attending conditions. In the auditory-ignoring condition, participants ignored all binaural auditory stimuli and were instructed respond to the short latency phase change in the Gabor patch. In the first auditory-attending condition, participants were instructed to attend to the ear in which the DPOAEs were recorded and to report a short-duration tone, while ignoring contralateral auditory stimuli and the visual Gabor patch. In the second auditory-attending condition, participants were instructed to report detection of a short-duration tone presented to the contralateral ear, while ignored the auditory stimulus in the DPOAE-recorded ear and the Gabor patch.

Figure 2.

Individual DPOAE contours for ten participants recorded during three attending conditions. DPOAE recorded during the visual attention condition, while ignoring all auditory stimuli in both ears (solid blue line); DPOAE recorded while attending to primary tones presented in the recorded ear, while ignoring tones presented to the contralateral ear and visual Gabor patches (solid-red line), and while attending to the primary tones presented to the contralateral ear, and ignoring the tones presented to the recorded ear and ignoring the visual Gabor patches (dashed-red line). The right (RE) or left (LE) recorded ear, DPOAE

frequency and handedness of the participant (RH: right handed, LH: left handed) are also indicated.

Figure 3.

Difference in absolute overall DPOAE onset level, from the visual attending condition in the auditory attend ipsilateral ear condition and in the auditory attend contralateral ear condition for each subject.

Figure 4.

Average DPOAE contours for ten participants recorded during three attending conditions. DPOAE recorded during the visual attention condition, while ignoring all auditory stimuli in both ears (solid blue line); DPOAE recorded while attending to primary tones presented in the recorded ear, while ignoring tones presented to the contralateral ear and visual Gabor patches (solid-red line), and while attending to the primary tones presented to the contralateral ear, and ignoring the tones presented to the recorded ear and ignoring the visual Gabor patches (dashed-red line).