Aging of the medial olivocochlear reflex and associations with speech perception

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The medial olivocochlear reflex (MOCR) modulates cochlear amplifier gain and is thought to facilitate the detection of signals in noise. High-resolution distortion product otoacoustic emissions (DPOAEs) were recorded in teens, young, middle-aged, and elderly adults at moderate levels using primary tones swept from 0.5 to 4 kHz with and without a contralateral acoustic stimulus (CAS) to elicit medial efferent activation. Aging effects on magnitude and phase of the $2f_1$ - f_2 DPOAE and on its components were examined, as was the link between speech-in-noise performance and MOCR strength. Results revealed a mild aging effect on the MOCR through middle age for frequencies below 1.5 kHz. Additionally, positive correlations were observed between strength of the MOCR and performance on select measures of speech perception parsed into features. The elderly group showed unexpected results including relatively large effects of CAS on DPOAE, and CAS-induced increases in DPOAE fine structure as well as increases in the amplitude and phase accumulation of DPOAE reflection components. Contamination of MOCR estimates by middle ear muscle contractions cannot be ruled out in the oldest subjects. The findings reiterate that DPOAE components should be unmixed when measuring medial efferent effects to better consider and understand these potential confounds.

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I. INTRODUCTION

The mammalian auditory efferent system originates in the auditory cortex and terminates in the cochlea via various nuclei along the brainstem (Guinan, 2006, 2010). The final branch of this efferent pathway courses between the lateral and medial olivocochlear nuclei and the cochlea. Of interest here is the medial olivocochlear (MOC) bundle, which consists of large-diameter, myelinated fibers terminating directly on outer hair cells (OHCs). When activated, the MOC efferents modulate gain of the cochlear amplifier via cholinergic channels; their influence on the cochlea is understood to be primarily inhibitory. MOC efferent activation has been shown to attenuate the magnitude of basilar membrane motion (Cooper and Guinan, 2006) and reduce the compound action potential while enhancing the cochlear microphonic (e.g., Delano *et al.*, 2007). Due to their non-invasive nature, otoacoustic emissions (OAEs) have been used to explore efferent-based modulation of cochlear mechanics in

humans (see Abdala *et al.*, 2009, 2013; Deeter *et al.*, 2009 for recent examples from this group).

In non-human animals, auditory efferents provide protection from the toxic effects of noise (e.g., Maison *et al.*, 2013) and are implicated in selective attention (Delano *et al.*, 2007). In humans, the auditory efferent system is active in sound localization in noise (Andeol *et al.*, 2011) as well as in perceptual learning (de Boer and Thornton, 2008). The role of the auditory efferents in facilitating speech perception in noise (de Boer *et al.*, 2012; Kumar and Vanaja, 2004) and mediating attention-related modulation of cochlear function (e.g., Garinis *et al.*, 2011a; Maison *et al.*, 2001) has also been explored.

In particular, the contribution of the medial efferent pathway to speech recognition received much attention following reports of improved signal detection-in-noise in cat (e.g., Kawase and Liberman, 1993). Giraud *et al.* (1997) demonstrated improved speech-in-noise intelligibility in the presence of contralateral acoustic stimulation (CAS) in human subjects, though this improvement was not observed in individuals who had undergone a vestibular neurectomy. The enhancement was correlated with the MOC reflex measured as CAS-induced reductions in transient-evoked otoacoustic emissions (TEOAE) amplitude. The role of the auditory efferent system in the detection of speech presented

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under noisy conditions has been re-evaluated over the years with mixed results. In almost every case the approach has been correlational; that is, speech-in-noise performance in a group of individuals has been correlated with their own CAS-induced changes in OAE magnitude. Kumar and Vanaja (2004) demonstrated a positive correlation, showing that individuals with bigger CAS-induced alterations in OAE magnitude performed better on a speech perception task. Others have reported the opposite effect (Michey et al., 1995; Garinis et al., 2011b). Most recently, de Boer and Thornton (2007) suggested that the efferent system plays a role in speech perception through dynamic control of cochlear gain, influenced by attention or experience.

The time line for age-related decline of auditory efferent function has been explored to a limited extent using OAEs. Castor et al. (1994) were the first to report a reduced influence of CAS on TEOAEs in a group of older adults (70–88 yr). In comparing DPOAE-based contralateral inhibition in three age groups, Kim et al. (2002) found medial efferent effects on DPOAEs to be reduced in the middle-aged (38–52 yr olds) as compared to the young adult group without any significant difference in the baseline DPOAE levels. This suggests the efferent auditory system exhibits age-related declines prior to notable degradation of OHC function. The conclusion has since been bolstered by similar results in mice (Fu et al., 2010; Jacobson et al., 2003; Zhu et al., 2007).

Aging effects on the MOC reflex have been linked to various sources. C57 mice, long used as a model for presbycusis, show declines in efferent inhibition with aging and a concomitant reduction in the neural population of the trapezoid body nuclei (Zhu et al., 2007). Recent work has shown aging-related declines in the MOC-OHC synaptic terminals in C57 mouse, independent of OHC loss (Fu et al., 2010). In CBA mice, decline in the expression of the channel protein Kv3.1b has been observed in MOC nuclei, with an associated functional decrease in the MOC reflex as measured by DPOAE suppression (Zettel et al., 2007).

To study DPOAE-based measures of the MOC reflex in humans, it is important to “unmix” the dual sources contributing to the DPOAE measured in the ear canal (Shera and Guinan, 1999; Talmadge et al., 1999). This unmixing approach is necessary because efferent activation differentially affects the two components of the DPOAE (Abdala et al., 2009, 2013; Deeter et al., 2009; Henin et al., 2011), termed here *distortion* (generated at the overlap of primary tones) and *reflection* (produced near the characteristic DP place, $2f_1\text{--}f_2$). The medial efferent system produces a stronger inhibitory effect on the magnitude of the DPOAE reflection component and alters its phase without affecting phase of the distortion component. Hence, at minima in DPOAE fine structure (where the two components are in phase cancellation), the differential effect of medial efferent activity can produce an enhancement of DPOAE magnitude by releasing this phase cancellation. As such, CAS-induced DPOAE level enhancement often reflects artifactual component-mixing rather than direct action of the MOC reflex.

The objective of this study was to examine changes in the MOC reflex associated with human aging across a six-decade span. We applied a comprehensive set of measures

TABLE I. Detailed demographic and testing information for each age group.

Age group	N	Gender		Ear		Age (yrs)	
		M	F	R	L	mean	range
Teen	27	14	13	17	10	15.5	13–17
Young adult	34	6	28	20	14	21.2	19–27
Middle-aged	22	4	18	12	10	48.7	40–58
Elderly	35	12	23	19	16	68.5	63–73

that considered effects of CAS on magnitude and phase of ear canal DPOAE as well as on its separated components; and probed the relationship between the MOC reflex and speech perception in noise in the aging ear.

II. METHODS

A. Subjects

Subjects included 118 individuals in four age groups: 27 teens, 34 young adults, 22 middle-aged adults, and 35 elderly adults (see Table I for details). Some subjects in the elderly group had audiometric thresholds outside of the normal range though within the expected range for their age (Gordon-Salant, 2005; see Fig. 1). Elderly subjects were recruited from an established subject registry at Northwestern University (NU) and by email solicitation at the House Research Institute (HRI). Elderly subjects were included for participation only if they presented with audiometric thresholds ≤ 35 dB hearing level (HL) at frequencies below 2 kHz and ≤ 65 dB HL between 3 and 8 kHz. Teen, young-adult and middle-aged subjects were recruited by verbal and email solicitation to HRI and House Clinic

FIG. 1. Audiograms for 35 individuals in the elderly group. The typical and atypical subgroups are designated by line, and the grand mean is superimposed. Atypical elderly had slightly elevated mean thresholds compared to typical elderly; relative threshold elevation ranged from 0.7 dB (at 6 kHz) to 5.3 dB (at 1 kHz).

employees and families, and by posted flyers. All had audiometric thresholds ≤ 15 dB HL.

As data analysis was initiated, the elderly group was further sub-divided into typical and atypical responders because a subset of older adults exhibited pronounced DPOAE fine structure upon the presentation of CAS (see Fig. 6 for an example). No other age group showed this pattern. Hence, elderly subjects were assigned to the atypical group if three or more of their DPOAE fine structure oscillations *increased* in peak-to-trough depth by ≥ 3 dB upon presentation of CAS at 60 dB sound pressure level (SPL). Ten out of 35 elderly subjects were labeled as atypical. These subjects were not included in the calculation of the MOC reflex because reductions in OAE level at fine structure peaks could not be calculated in this group. However, their data are analyzed in comparison with the typical elderly and considered in the discussion section.

B. DPOAE Protocol

Adult subjects were tested at HRI and NU. Teens were tested exclusively at HRI. The test ear was chosen at random unless one ear had markedly better DPOAE levels. Subjects were awake during testing and seated comfortably in a padded armchair within a double-walled IAC sound-attenuating chamber. Air conduction hearing thresholds were determined using a standard Hughson-Westlake audiometric procedure between 250 and 8000 Hz.

Stimulus tones, f_1 , f_2 , were presented at 65 and 55 dB SPL (L_1 , L_2) with a fixed f_2/f_1 ratio of 1.22. Primary tones were logarithmically swept upwards in frequency at 8 s/octave to yield $2f_1-f_2$ DPOAEs between 500 and 4000 Hz. Twelve to 16 sweeps were collected in the no-noise condition (NoN) to form two averages of six to eight sweeps each, providing an index of natural response variability. Six to eight sweeps were collected with broadband noise (CAS) presented at 60 dB SPL in the opposite ear via an ER2 insert transducer. The CAS was turned on 1 s before the primary tones and there was a 2-s interval between sweeps. CAS elicitors of 65 and 70 dB SPL were also presented during this protocol but not used to calculate the MOC reflex. The frequency response of contralateral noise (re: Zwislocki coupler) was relatively flat between 0.2 and 12 kHz. The NoN and CAS sweeps were interleaved in pairs throughout the test protocol in a repeating sequence until the target number of sweeps had been presented.

C. Signal processing and instrumentation

DPOAEs were recorded using a Macintosh laptop controlling a MOTU 828 Mk II audio device (44.1 kHz, 24 bit). The output of the MOTU was appropriately amplified and routed to either MB Quartz 13.01 HX drivers (NU) or Etymotic Research ER-2 insert phones (HRI). The output of the drivers was coupled to the subjects' ears through the sound tubes of an Etymotic Research ER10B+ probe microphone assembly.

DPOAE level and phase estimates were calculated using a least-squares-fit algorithm (LSF) at frequency intervals between 2 and 18 Hz. As an initial data inclusion criterion, a

median of every three consecutive points in the average was calculated and compared to the noise estimate at the corresponding frequency; if the signal-to-noise ratio (SNR) was < 6 dB, the data point was not accepted. Each average included a total of ~ 400 –500 individual data points spanning the three-octave test range. In this implementation of the LSF technique, models for the stimulus tones and DPOAE of interest are created. Signal components were then fitted to these models to minimize the sum of squared errors between the model and the data (Long *et al.*, 2008). Our implementation of the LSF used 500 ms overlapping windows shifted in 50 ms steps. The noise floor was estimated by taking the difference between sweep pairs and applying the LSF to this difference. DPOAE phase was unwrapped by sequentially subtracting 360° from all points beyond identifiable discontinuities. The final estimate of DPOAE phase was computed by subtracting $2\phi_1 - \phi_2$, (where $\phi_{1,2}$ are phases of f_1 and f_2) from ϕ_{dp} (the extracted phase at $2f_1 - f_2$).

D. Component separation: Inverse FFT

MATLAB-based software was used to separate the DPOAE distortion and reflection components based on their respective phase-gradient delays (developed by C. Talmadge, adapted by P. Luo). During inverse FFT (IFFT), the DPOAE complex pressure measured in the frequency domain was multiplied by a moving Hann window in overlapping 50 Hz steps. The bandwidth of the window was adjusted on a logarithmic scale and ranged from 400 to 960 Hz as frequency increased. Rectangular time-domain filters were applied to each window to recursively extract the target component. A search range of -2 to 10 ms was applied to window the distortion component, and 3 to 15 ms to window the main reflection component from the DP place ($2f_1 - f_2$). Time domain filters were centered around the peak energy within each window. The main reflection component was also separated from longer-latency reflection (LLR), likely associated with multiple internal reflections (Dhar *et al.*, 2002). Filtered windows of data were then transformed back to the frequency domain by FFT and the level and phase of the distortion and reflection components reconstructed. Data segments equal to half of the length of the analysis window were eliminated at low- and high-frequency boundaries to remove edge effects caused by the time-windowing process.

E. Speech perception protocol

Speech testing was conducted at easily audible levels using custom-developed software (ISTAR and ICAST; Fu *et al.*, 2005). Speech tokens were presented at 30 dB above speech reception thresholds (SRTs) but never lower than 60 dB SPL. Vowel identification was tested using 12 vowels presented in /h/V/d/ context, i.e., a vowel embedded between the consonants /h/ and /d/ (had, hod, hawed, head, hayed, heard, hid, heed, hoed, hood, hud, and who would) produced by three male and three female talkers for a total of 72 stimuli. Consonant identification was tested using 20 consonants presented in /a/C/a/ context, i.e., a consonant bracketed by

the vowel /a/ (aba, ada, aga, apa, ata, aka, ama, ana, ala, ara, aya, awa, afa, asa, asha, ava, aza, atha, acha, aja) for a total of 120 stimuli. A stimulus was randomly selected and presented to the subject ipsilaterally via an ER2 insert phone at SNRs ranging from -21 to $+12$ dB in 3 dB steps until asymptotic performance was reached. Speech level was kept constant while noise level was changed to produce the desired SNR. The subject used the computer mouse to select one of the 12 vowel choices or 20 consonant choices shown onscreen in a grid. A new stimulus was not presented until a response was recorded; no feedback was given.

Word-in-sentence recognition was measured using sentences from the Hearing in Noise Test (HINT) (Nilsson *et al.*, 1994). The HINT corpus contains 26 lists of 10 sentences each, for a total of 260 sentences. Two lists were presented in each SNR condition. The subject repeated as many words as he/she heard, and the experimenter noted the correctly identified words. The entire speech sequence required from three to five hours and was conducted in multiple sessions.

Once the percentage of correctly identified syllables/words was calculated at each SNR, a performance-intensity (PI) function was plotted. Speech results were quantified in three ways: (1) The slope of the PI function between 20%–80% correct for each type of speech token, (2) the SNR required to achieve 25%, 50%, and 75% correct for each type of speech token, and (3) feature analyses calculating overall percent-correct for consonant and vowel tokens separately as well as percentage of information transmitted for manner, voicing, place, height, duration features (Miller and Nicely, 1955).

F. Calibration

To record DPOAEs, calibrated stimuli were delivered to each subject after compensating for the depth of probe insertion (Lee *et al.*, 2012). This allowed us to approximate the desired SPL across frequency at the tympanic membrane and in doing so, mitigate the effects of standing waves. Broadband noise level was calibrated in an ear simulator (IEC 60318-4; Bruel and Kjaer 4157). Sound pressure levels for speech material were initially calibrated by measuring the long-term RMS of a repeating /a/ vowel through an ER2 earphone in a Zwislocki coupler connected to a sound level meter (SLM) (A weighting). The amplifier output was adjusted to achieve levels on the SLM ranging from 40 to 85 dB SPL in 5 dB steps, and the associated voltage noted. Before each test session, the voltage of a 1 kHz tone was adjusted to the value associated with the desired test level (determined by each subject's own SRT).

G. Analysis

1. The MOC reflex

The first three MOCR measures described below (a)–(c) were taken at DPOAE fine structure maxima only to minimize the effect of component mixing. Maxima were identified based on the first and second derivatives of the DPOAE level function and the relationship between them. Data

points where the first derivative was equal to zero and the second derivative was negative were identified as local maxima (see Abdala and Dhar, 2012).

- (a) $\text{MOCR}_{\text{dB}} = L_{\text{dp}}^{\text{CAS}} - L_{\text{dp}}^{\text{NoN}}$, where L_{dp} is DPOAE level. For MOCR indices, we restricted ourselves to measuring *reductions* in level (termed here *inhibition* and shown as negative values). Episodes of CAS-induced enhancement were defined as $\geq +0.1$ dB change from baseline level and were reported separately. Evidence suggests different mechanistic origins for CAS-induced enhancement compared to reduction in DPOAE level (Abdala *et al.*, 2009). We implemented this analysis strategy in an attempt to disentangle true MOC effects from artifacts related to component mixing.
- (b) $\text{MOCR}_n = (|P_{\text{dp}}^{\text{NoN}}| - |P_{\text{dp}}^{\text{CAS}}|) / |P_{\text{dp}}^{\text{NoN}}|$, where $|P_{\text{dp}}|$ is the magnitude of the complex DPOAE measured in the ear canal. MOCR_n was reported as a fraction of the baseline magnitude.
- (c) $\text{MOCR}_{\text{vn}} = |(P_{\text{dp}}^{\text{CAS}} - P_{\text{dp}}^{\text{NoN}})| / |P_{\text{dp}}^{\text{NoN}}|$, where P_{dp} is the complex DPOAE pressure. MOCR_{vn} was calculated as the magnitude of the difference vector between NoN and CAS conditions and reported as a fraction of the baseline magnitude.
- (d) $\text{MOCR}_{\text{Dn}}, \text{MOCR}_{\text{Rn}} = (|P_{\text{D}}^{\text{NoN}}| - |P_{\text{D}}^{\text{CAS}}|) / |P_{\text{D}}^{\text{NoN}}|$ and $(|P_{\text{R}}^{\text{NoN}}| - |P_{\text{R}}^{\text{CAS}}|) / |P_{\text{R}}^{\text{NoN}}|$, where $|P_{\text{D}}|$ and $|P_{\text{R}}|$ represent distortion and reflection-component magnitudes respectively. MOCR_{Dn} and MOCR_{Rn} are reported as a fraction of the baseline magnitude.
- (e) $\text{MOCR}_{\text{pA}} = (\phi^{\text{CAS}}(0.7) - \phi^{\text{CAS}}(3.6)) - (\phi^{\text{NoN}}(0.7) - \phi^{\text{NoN}}(3.6))$. The phase accumulation in cycles between $f_{\text{dp}} = 0.7$ and 3.6 kHz was measured as an approximate metric of phase slope for the reflection component. The difference in phase accumulation between NoN and CAS conditions was calculated.

2. Statistical analyses

a. Age effects. So as to maximize usage of all data points for the repeated measures variable, frequency was collapsed into low- and high-frequency categories (1414 Hz cutoff) for analyses of variance (ANOVA) tests; however, Figs. 3–5 display MOCR data at each third-octave center frequency to provide the reader with detailed frequency information. Age (4) $\times$ frequency (2) ANOVAs with repeated measures on frequency were conducted for each of the primary MOCR indices (SPSS ver. 18.0). The ANOVA F and p values are provided in the figure captions. When appropriate, *post hoc* age contrasts were conducted using a Bonferroni correction. Additional ANOVAs were conducted to assess LLR level as a function of CAS in the elderly group. The alpha level was set at $p < 0.05$.

Phase-frequency functions were fit with loess lines in both CAS and NoN conditions. To reduce non-meaningful phase variance, functions with phase values that were not within ± 0.5 cycles of zero at 0.7 kHz were shifted up or down by one cycle. Since all frequency points are shifted by the same integer value, the normalization procedure does not

affect the frequency-dependent phase accumulation measured in any one subject, but simply reduces the scatter that comes from an offset of the first point.

b. Speech analyses. Pearson Product Moment correlations were conducted between five MOCR measures: MOCR_n , MOCR_{Vn} , MOCR_{Dn} , MOCR_{Rn} taken at 1122 Hz (the center frequency producing the most robust reflex overall), MOCR_{PA} and three indices of speech-in-noise performance: (1) slope of the PI function, (2) the SNR required to achieve 25, 50, and 75% correct, and (3) overall percent-correct scores for consonant and vowels, as well as standard metrics of information transmitted for the following speech features: height, duration, place, voicing, and manner. The alpha level for correlations was set at $p < 0.01$.

III. RESULTS

DPOAE level and noise floor data were averaged into third-octave bins with center frequencies of 707, 891, 1122, 1414, 1781, 2245, 2828, and 3563 Hz. The average SNR for each age group was determined by calculating the difference between noise and DPOAE levels at each center frequency, then averaging these values across frequency. Average DPOAE SNR values for each age group in NoN and CAS, respectively, were as follows: teens, 28, 29 dB SPL; young adults, 29, 28 dB SPL; middle-aged adults, 26, 23 dB SPL; and elderly, 20, 19 dB SPL. These data indicate that the MOC indices, which are measured as difference scores and thus

influenced by independent variance in both NoN and CAS conditions, were calculated using DPOAE data with strong noise immunity. Consistent with past work, episodes of DPOAE enhancement (versus the more commonly observed reductions in level) accounted for $<10\%$ of MOCR measures in all age groups as follows: teens, 3.5%, young adults, 8%, middle-aged adults, 4.6%, and elderly, 7.2%.

A. The MOC reflex and age

Figure 2 shows one individual example of DPOAE level fine structure in NoN and CAS at 60 dB SPL for each age group. The inset in each figure shows two NoN averages to display normal run-to-run variability for each subject, and to illustrate that CAS-induced changes exceeded this variability. Figure 3 displays the mean MOCR_{dB} for the four age groups, and standard error of the mean (SEM). Although the MOCR metric in dB was not statistically analyzed, it is provided here for comparison to past work. The mean reflex ranged from ~ 0.5 to just over 2 dB and was strongest in the low-frequency range for all but the elderly group. The elderly group showed the largest CAS effect overall and relatively equal reductions in emission level across frequency.

Figures 4(A) and 4(B) show the metrics normalized by baseline magnitude, MOCR_n and MOCR_{Vn} for the four age groups. Main effects of age and frequency were observed on MOCR_n along with an interaction between the two (see figure captions for F and p values). Age contrasts confirmed that middle-aged adults had weaker reflexes than both elderly

FIG. 2. Individual examples of DPOAE fine structure in no-noise (NoN) and during contralateral acoustic stimulation (CAS) at 60 dB SPL for each of the four age groups. The inset in each group shows two superimposed NoN averages and illustrates the typical level variability.

FIG. 3. Mean DPOAE medial olivocochlear reflex in dB ($MOCR_{dB}$) and standard error of the mean (SEM) for the four age groups plotted at third-octave intervals. Although data are shown at individual center frequencies, frequency was collapsed into low and high categories (1414 Hz boundary) for statistical testing. Negative values indicate reductions in DPOAE level with CAS; the dashed line represents no level change.

($p=0.005$) and young adult groups ($p=0.05$) for frequencies < 1414 Hz. Above 1414 Hz, the elderly group showed larger reflexes than all other age groups ($p < 0.001$ for the three age contrasts). $MOCR_{Vn}$ also showed main effects of age and frequency but no interaction. *Post hoc* age contrasts confirmed that elderly subjects had larger $MOCR_{Vn}$ than teens ($p < 0.0001$) and middle-aged adults ($p = 0.001$).

The MOC reflex was examined for distortion ($MOCR_{Dn}$) and reflection ($MOCR_{Rn}$) components separately as shown in Figs. 5(A) and 5(B). Results are consistent with several previous studies showing that MOC activation reduces the reflection more than distortion component of the DPOAE. Distortion is reduced by approximately 5% to 18% of baseline amplitude on average across frequency; reflection, between 10% to 34% on average. Both components showed main effects of CAS on age and frequency, the elderly group manifesting the strongest MOC reflex. $MOCR_{Dn}$ showed an interaction between age and frequency; hence, *post hoc* age contrasts were conducted and elucidated two trends: (1) The $MOCR_{Dn}$ measured from the elderly group was larger than each of the other age groups for frequencies above 1414 Hz ($p < 0.0001$ all age contrasts) and (2) the middle-aged group showed weaker MOC reflexes than both elderly and young adult groups ($p = 0.009$; $p = 0.012$, respectively) for frequencies below 1414 Hz.

Two consistent patterns emerging from these analyses on emission magnitude are (a) the elderly group shows the strongest reflex across frequency; (b) the middle-aged group shows weakened MOC reflexes in the low frequencies (< 1414 Hz).

CAS-induced changes in reflection-component phase were examined for age trends. Delays calculated from stimulus frequency OAEs, also reflection-type emissions, have

FIG. 4. Mean DPOAE medial olivocochlear reflex (A) normalized by baseline magnitude ($MOCR_n$) and (B) as magnitude of the difference vector ($MOCR_{Vn}$) for the four age groups plotted at third-octave intervals. Frequency was collapsed into low and high categories (1414 Hz boundary) for statistical testing. Error bars represent the SEM. For $MOCR_n$, significant age ($F = 10.4$; $p < 0.0001$) and frequency effects ($F = 40.4$; $p < 0.0001$) were observed and an interaction ($F = 4.9$; $p = 0.003$); for $MOCR_{Vn}$, significant age ($F = 7.9$; $p < 0.0001$) and frequency effects ($F = 35.5$; $p < 0.0001$) were observed but no interaction.

been shown to predict cochlear tuning (Shera *et al.*, 2002). All four age groups showed mild shallowing of the phase slope (filled with loess trend lines; Cleveland, 1993) once CAS was introduced consistent with shorter delays and broadened tuning. This change was quantified by calculating phase accumulation between 0.7 and 3.6 kHz. The CAS reduced phase accumulation significantly ($F = 17.7$; $p < 0.0001$) but there was no effect of age on phase accumulation nor an interaction.

B. Atypical elderly subjects

Figure 6 illustrates an example of the impact of 60 dB SPL CAS on DPOAE fine structure in a subset of 10 atypical elderly subjects (who were not included in group calculations of the MOC reflex). In this subgroup, CAS did not evoke typical effects on DPOAE level or phase; rather, it

FIG. 5. Mean (A) distortion- ($MOCR_{Dn}$) and (B) reflection-component ($MOCR_{Rn}$) MOC reflex normalized by baseline magnitude for each of the four age groups and plotted at third-octave intervals. Error bars represent the SEM. There were significant effects of age for both indices ($MOCR_{Dn}$: $F = 7.6$, $MOCR_{Rn}$: $F = 8.2$; $p < 0.001$ both) and frequency ($MOCR_{Dn}$: $F = 107.4$, $MOCR_{Rn}$: $F = 23.3$; $p < 0.0001$ both). $MOCR_{Dn}$ also showed an interaction: $F = 3.3$; $p < 0.024$.

created more pronounced fine structure, primarily below 2 kHz as noted in Fig. 6, and produced *steeper* reflection-component phase slope, i.e., more phase accumulation between 0.7 and 3.6 kHz. 60% of the typical elderly subjects also showed CAS-induced deepening of DPOAE fine structure but only at higher contralateral noise levels (65 and 70 dB SPL). No other age group showed these effects.

The origin of this atypical DPOAE response to contralateral noise is not known but one hypothesis is that the middle ear muscle reflex (MEMR) was evoked by the contralateral elicitor. In general, DPOAE fine structure becomes more pronounced as the magnitude difference between distortion and reflection components decreases. This can be achieved if the contribution of intracochlear reflection (which at moderate primary levels typically contributes less than distortion to the DPOAE mixture) increases. Activation of MEM contractions, and concomitant

FIG. 6. DPOAE fine structure in NoN and CAS at 60 dB SPL recorded from one atypical elderly adult. In this group of elderly (not used for calculation of MOC reflexes), the presentation of CAS produced more pronounced fine structure, even at the lowest CAS levels (60 dB SPL).

stiffening of the ossicular chain, would augment the impedance mismatch at the basal boundary between the cochlea and the middle ear, thereby increasing the proportion of reverse-traveling emission energy reflected back into the cochlea. This would in turn set up additional reflections with longer delays, i.e., multiple internal reflections (MIRs) (Dhar *et al.*, 2002). Thus, a MEM reflex activated by contralateral noise could produce an increase in reflection and a corresponding increase in DPOAE fine structure completely independent of any influence of the MOCR on DPOAEs. To probe the plausibility of this hypothesis, longer-latency reflection was analyzed as a function of CAS level for both typical and atypical elderly groups.

Figure 7(A) shows mean level of the main reflection at $2f_1-f_2$ as a function of CAS level; there appears to be no systematic increase associated with CAS though the atypical group shows a trend towards increasing reflection as CAS increases. Figure 7(B) shows mean levels of the longer-latency reflection, which does increase as contralateral noise increases, most notably for the atypical elderly. The magnitude of LLR was not systematically influenced by CAS in any of the other age groups. A one-way ANOVA conducted on LLR level revealed a significant effect of CAS for the atypical elderly group only ($F = 8.81$; $p = 0.0003$) and no significant effect of CAS on LLR for typical elderly although this group shows a trend toward increasing LLR [see Fig. 7(B)—black bars].

Figure 8 displays additional phase accumulation (re: main reflection) for the LLR component. As expected, all age groups show three to four additional cycles of phase due to the later time windowing of these LLRs. However, only the elderly showed increased phase accumulation (~ 1.5 cycles) when CAS was presented, consistent with an increase in multiple internal reflections.

To probe whether the observed increases in LLR induced by CAS were due to changes in middle-ear impedance associated with MEMRs, we attempted to correlate changes in the LLR with changes in the ear-canal level of the f_1 primary tone (i.e., L_1). Changes in primary tone level

FIG. 7. Total reflection-component energy measured from time domain filters centered to estimate energy (A) at the DP place ($2f_1-f_2$) which is considered the main reflection site and (B) associated with longer latencies (LL), presumably related to multiple internal reflections. Both DP place and LL reflection is shown in NoN and at three levels of contralateral noise (CAS) for both the typical and atypical elderly groups. Neither group shows systematic changes in DP-place reflection once CAS is introduced; the atypical subset shows statistically significant increases in LL reflection with increases in CAS. Error bars represent SEM.

have previously been used as a gauge of MEM contractions (Guinan, 2006; Henin and Long, 2012). Although we suspected that probe fit was not monitored here with the rigor required to detect such small changes in L_1 (as small as 0.12 dB or 1.4% change in amplitude), our hope was to test for correlations between CAS-induced changes in L_1 and changes in the magnitude of LLR, both calculated in 200 Hz frequency bands centered around the largest L_1 shift induced by CAS. Unfortunately, we found that the sweep-to-sweep variability of our elderly data at both CAS = 60 and 70 was too large to reliably quantify CAS-induced changes in either variable. Any correlation between the two, if present, was masked by this variability.

In sum, our analyses indicate that CAS produced marked changes in DPOAE fine structure, steepened reflection-component phase and increased LLR in the elderly group only, most notably in a subgroup of atypical elderly. The source of these effects is not known. We hypothesize

FIG. 8. The additional phase periods accumulated (re: main reflection at $2f_1-f_2$) for longer-latency reflection. All age groups show additional phase accumulation for the later component (as expected because of the time-domain filters utilized), but only the elderly groups, and most notably the atypical elderly, show increased phase accumulation when CAS was presented. This result is consistent with multiple internal reflections. Error bars represent SEM.

that CAS-induced MEM contractions may have contributed to the results.

C. Speech tests

It was not the objective of this study to examine how speech perception changes with age. Correlational statistics were conducted preliminarily simply to verify previously documented results of decreasing speech-in-noise performance with aging (e.g., Dubno *et al.*, 1984). All correlations between age and speech-test performance were significant; the older the individual, the poorer the performance on speech-in-noise tests. However, if subjects >60 yr were eliminated from the analysis, there were no significant correlations between age and speech scores.

More to the point of the present study, initial correlations were conducted between speech scores and MOCR indices. Only one of five MOCR indices, MOCR_{VN}, showed significant correlations with speech results but these correlations were present only when elderly subjects (>60 yr old) were included. The correlations were unexpectedly positive, indicating that reduced speech performance was associated with a stronger MOC reflex. This pattern can likely be explained by the shared association of age with both speech perception and MOCR: Elderly subjects showed the largest MOCR values and the poorest speech perception scores, hence, poor speech perception was correlated with large MOCR values. Their common link to age likely drove this correlation. This is supported by the fact that once subjects >60 yr of age were excluded, there were no significant correlations between MOCR and speech.

With elderly subjects eliminated, speech performance was parsed into speech features to further probe the relationship between speech-in-noise performance and MOC reflex

* Speech features are measured by "information transmitted" (Miller & Nicely, 1955) not in percent correct

FIG. 9. There were ten significant positive correlations between indices of the MOCR reflex and performance on vowels and consonants (overall percent-correct), as well as the effectiveness in transmission of speech feature information at 0 and -3 dB SNR. These correlations were conducted without the elderly subjects, and included data from individuals ranging from 13 to 58 years of age.

for a restricted age range, 13–58 years. The speech features explored were as follows: (1) vowels—overall percent correct, place, height, and duration; (2) consonants—overall percent correct, voicing, manner, and place. Speech performance at four SNRs (0, -3 , -6 , and -9) was correlated with five MOCR indices for a total of 160 correlations. Ten of these were significant, all of which included MOCR indices based on either ear canal DPOAE or distortion-component metrics (MOCR_{Dn} or MOCR_n); the better the speech test performance (or the greater the information transmission for a specific feature), the larger the MOCR (see Fig. 9).

IV. DISCUSSION

A. Aging of the MOC reflex

The effect of aging on human DPOAE and component-based measures of the MOC reflex will first be considered without the oldest subjects. Results indicate mild aging of the MOC reflex through middle age. Middle-aged subjects had weaker MOC reflexes than young adults for the normalized DPOAE ear canal metric (MOCR_n) and for the distortion component (MOCR_{Dn}) below 1500 Hz. Unlike earlier work, our findings indicate that aging of the MOCR through mid-life is not robust. The age effect was not consistently present across frequency nor DPOAE components. Additionally, measures of component phase were insensitive to this aging trend. Although all age groups showed a CAS-induced shallowing of reflection-component phase slope consistent with model predictions of broadened tuning by medial efferent activation (Guinan, 1986), it did not vary with age.

This relatively mild MOCR aging effect differs from past results, likely due to differences in the categorization of age and in overall methodology. None of the past work on aging of the MOCR considered the dual-source nature of DPOAEs and how component interaction influences measures of the medial efferent reflex, i.e., how the effect of an MOCR elicitor differentially impacts each DPOAE source (Abdala *et al.*, 2009; Deeter *et al.*, 2009). MEM reflexes were not always monitored in past work although evidence suggests they change with aging (Jerger *et al.*, 1978; Jerger, 1979) and have been observed at moderate CAS levels (Henin and Long, 2012).

The source of aging on the MOCR is not well understood. Studies using an accelerated-aging mouse model have shown an aging effect on MOC-OHC synapses in the C57 mouse between 2 and 12 postnatal months (Fu *et al.*, 2010). MOC terminals were diminished by up to 65% even with normal OHCs or no more than mild OHC loss. If this age-related observation can be extended to humans, it suggests that our middle-aged group with clinically normal thresholds (and presumably normal or near-normal OHC counts and function) might have an independent loss of medial efferent synapses and a functional decline in the MOC reflex and its ability to modulate cochlear amplifier gain. However, this alteration if present in the middle-aged group, produced only mild aging effects on AO measures of the MOC reflex.

B. Atypical results in elderly

Contralateral broadband noise produced unexpected results in the oldest subjects. The elderly group was subdivided into what we termed typical and atypical responders based on the effects of CAS on DPOAE fine structure. Ten of the 35 elderly participants showed a pronounced increase in fine structure upon presentation of CAS at relatively low levels (60 dB SPL). This deepened fine structure was also noted in many typical elderly at higher CAS levels (65 and 70 dB SPL). In all, DPOAE fine structure from 25 of 35 elderly ears became more pronounced with deeper peak-to-trough values upon presentation of contralateral noise.

These CAS-induced increases in fine structure suggest increased component interference, which occurs when the

relative contributions of the two DPOAE components to the ear canal emission became more equal (often associated with increases in reflection). Indeed, analyses indicate CAS-induced increases in reflection energy in the atypical elderly, most notably *longer latency reflection* associated with MIRs. A heightened impedance mismatch at the junction between the cochlea and the middle ear could produce increases in MIRs. One hypothesis is that CAS-induced activation of MEM reflexes exacerbated this mismatch so that more of the outgoing emission energy was re-introduced into the cochlea, setting up additional instances of coherent reflection from the DPOAE characteristic frequency region and eventually contributing to a greater reflection component measured in the ear canal signal. This hypothesis could also explain the CAS-induced increases in magnitude and additional phase accumulation of longer-latency reflection in the elderly (both consistent with increasing MIRs) as well as the large MOC reflexes observed in elderly group. Combined tone and CAS presentation can be an inadvertent but potent elicitor of the MEMR. [Henin and Long \(2012\)](#) observed correlations between increases in efferent-mediated DPOAE suppression and MEM activation (as measured by changes in primary tone level and phase), confirming that middle-ear muscle contractions can augment measures of the MOC reflex.

It is not clear why CAS might be a more potent elicitor of middle ear muscle contractions in the elderly and not the younger groups. In general, past studies investigating aging effects on the MOCR ([Kim et al., 2002](#)) tested elderly subjects with normal thresholds in an attempt to separate intrinsic aging processes from sensory cell loss. We included elderly with mild-to-moderate amounts of hearing loss at some frequencies (see Fig. 1). Indeed, a subgroup of the current elderly cohort ($n = 18$) served as subjects in a separate study in our joint laboratories; they showed larger age-related decreases in the DPOAE distortion-component (which is linked to cochlear nonlinearity) and compression, than the reflection component. This finding indicates that older ears with some mild hearing loss may lose cochlear compression and become “linearized” with age. A reduced dynamic range and abnormal loudness growth could impact MEMRs.

Past work on the acoustic reflex and aging has been mixed, most of it conducted three decades ago using less sensitive probe microphones and analysis techniques. Some of these early studies reported that aging (in older individuals with normal audiometric thresholds) produced elevated stapedius muscle thresholds elicited by broadband noise ([Silman, 1979](#); [Gelfand and Piper, 1981](#); [Silverman et al., 1983](#)). Others found no such age-related elevation in MEM reflex thresholds or even reported decreases in middle ear muscle threshold in a group of elderly individuals ([Jerger et al., 1978](#); [Jerger, 1979](#)).

Contralateral noise has produced DPOAE level *enhancement* in aged mice ([Varghese et al., 2005](#)); however, this enhancement may be reflecting the same fine structure effect illustrated in Fig. 6. If components are not considered or separated, and one simply notes CAS-induced changes in ear canal DPOAE levels, it is easy to see how enhancement would be measured in some subjects. There are likely

multiple factors at play producing the unexpected results in elderly subjects, most notably in the small group of atypical responders. The MEMR may be one of these factors. As the focus of this work was not the MEMR, we did not include measures with adequate sensitivity nor monitor primary tone level with the needed rigor to detect small MEM contractions. Future work is warranted to study whether CAS-induced increases in longer-latency reflection might provide a useful metric of MEM contractions from an intracochlear versus traditional ear canal vantage point.

C. Relationships between MOCR and speech perception

Because of the co-existence of large measured MOC reflexes and reduced speech perception scores in the elderly, correlations between the two variables and age were not informative. Correlations between age and MOC indices in a restricted age range (13–58 yr) were significant, the distortion component of the DPOAE accounting for the greatest amount of variance in speech scores at SNRs of 0 and –3. Consistent with past work, the larger the MOCR the better transmission of place and manner information and the better the overall performance on both consonant and vowel recognition.

The correlations between speech and the MOCR were moderate, accounting for less than 40% of the variance in all instances; only 10 of 160 correlations were significant. There are several potential reasons for these limited associations: (1) Speech test performance did not vary greatly between 13 and 58 yr of age; as such, the needed systematic scatter in speech scores to detect robust correlations was likely lacking. (2) MOC activation was conducted by *contralateral* acoustic stimulation; this route is mediated by uncrossed MOC fibers, whereas speech perception tests were conducted presenting ipsilateral speech and noise to the test ear under the same earphone. Therefore, the route by which noise degraded the speech signal may not accurately probe the contralateral MOC reflex. (3) It would have been ideal to collect speech data concurrently with activation of the MOC, the same MOC elicitor producing the background noise during speech recognition tests. (4) We did not control for task-dependent factors such as selective attention, which has been shown to modulate medial efferent effects ([Froehlich et al., 1993](#); [de Boer and Thornton, 2007](#)). These issues may explain why links between speech perception and the MOCR were moderate at best, though in the expected direction.

V. CONCLUSIONS

To conclude, by middle age the contralaterally evoked MOC reflex is weakening for frequencies <1500 Hz where medial efferent effects are largest. The oldest subjects showed the strongest estimates of the MOC reflex. We hypothesize that interference from MEM contractions in the elderly may have contributed to this finding; preliminary analysis suggests this is a plausible hypothesis that warrants further study. Performance on tasks of speech recognition in noise and in the effectiveness of speech-feature transmission

is better in individuals with larger MOC reflexes, namely, those involving the distortion component which provides better SNR than reflection. Importantly, our results reiterate that study of the efferent system using the DPOAE must account for component mixing and measure the potentially intrusive effect of MEM contractions.

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