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Musicianship enhances ipsilateral and contralateral efferent gain control to the cochlea

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ABSTRACT

Human hearing sensitivity is easily compromised with overexposure to excessively loud sounds, leading to permanent hearing damage. Consequently, finding activities and/or experiential factors that distinguish "tender" from "tough" ears (i.e., acoustic vulnerability) would be important for identifying people at higher risk for hearing damage. To regulate sound transmission and protect the inner ear against acoustic trauma, the auditory system modulates gain control to the cochlea via biological feedback of the medial olivocochlear (MOC) efferents, a neuronal pathway linking the lower brainstem and cochlear outer hair cells. We hypothesized that a salient form of auditory experience shown to have pervasive neuroplastic benefits, namely musical training, might act to fortify hearing through tonic engagement of these reflexive pathways. By measuring MOC efferent feedback via otoacoustic emissions (cochlear emitted sounds), we show that dynamic ipsilateral and contralateral cochlear gain control is enhanced in musically-trained individuals. Across all participants, MOC strength was correlated with the years of listeners' training suggested that efferent gain control is experience dependent. Our data provide new evidence that intensive listening experience(s) (e.g., musicianship) can strengthen the ipsi/contralateral MOC efferent system and sound regulation to the inner ear. Implications for reducing acoustic vulnerability to damaging sounds are discussed.

1. Introduction

Intense acoustic environments can be hazardous to human hearing as overexposure to excessively loud sounds can result in permanent noise-induced hearing loss (NIHL). NIHL is second only to age-related hearing impairments (Rabinowitz, 2000) and accounts for more than $1 billion in medical costs in the USA (USDoVA, 2005). Indeed, it is estimated that ~26 million people suffer from some form of NIHL (NIH/NIDCD, 2008) and there is growing concern that recreational noise exposure (e.g., personal music players) may be increasing NIHL prevalence among the general population (Levey et al., 2012; WHO, 2015). Problematically, there is considerable inter-subject variability in vulnerability to noise exposure and acquiring cochlear injury due to excessively loud sounds (Cody and Robertson, 1983; Patuzzi and Thompson, 1991). Furthermore, transient (i.e., temporary) hearing losses due to less traumatic noise exposures do not predict progression to permanent acoustic injury (Ward, 1965). This variability has led to the speculation that some listeners might have "tough" ears that are more resilient to noise damage, while others have "tender" ears more sensitive to acoustic insult (Maison and Liberman, 2000). Consequently, identifying listening activities and/or experiential factors that predict or offset acoustic vulnerability (i.e., distinguish "tender" from "tough ears") could be important in identifying people at higher risk for developing NIHL and preventing certain recreational hearing damage.

In this regard, musical training has been shown to have profound impact on auditory skills, improving not only basic perceptual acuity for speech sounds but also the brain's ability to extract important communication signals from the auditory scene (for reviews, see Alain et al., 2014; Moreno and Bidelman, 2014; Strait and Kraus, 2014). Functional changes secondary to musical training have been observed in all stages of the auditory system from cerebral cortex (Bidelman and Alain, 2015; Bidelman et al., 2014b; Schneider et al., 2002; Shahin et al., 2003) to the auditory brainstem (Bidelman et al., 2011, 2014b; Musacchia et al., 2007;

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Wong et al., 2007), and as peripheral as the human cochlea (Bidelman et al., 2014a, 2016). Given the pervasiveness of musical engagement to benefit a wide variety of auditory (and non-auditory) skills, musicians are widely considered an ideal model for understanding the brain's capacity for neuroplasticity (Bidelman, 2016; Herholz and Zatorre, 2012; Kraus and Chandrasekaran, 2010; Moreno and Bidelman, 2014; Zatorre and McGill, 2005).

While musicianship has been shown to positively enhance certain aspects of auditory function, presumably, long-term music training could also produce detrimental consequences to hearing. Notably, musicians experience sound levels (>90–100 dBA) (Gopal et al., 2013; Møllerløkken et al., 2013; Royster et al., 1991; Schmidt et al., 2011) that regularly exceed recommended daily noise exposure levels (i.e., 85 dBA) (NIOSH, 1998). While most studies have focused on musical ensemble environments, excessive noise is also apparent during individual practice, when sound levels are exacerbated in smaller acoustic spaces (Poissant et al., 2012). Consequently, there is increasing concern that excessive exposure to intense sound levels during music rehearsal may be increasing the prevalence of noise-related hearing impairments among people who engage in music performance (Henning and Bobholz, 2016; Phillips et al., 2010). On the contrary, enduring higher sound levels over time may act to fortify (rather than impair) hearing through tonic engagement of reflexive pathways that help regulate sound transmission and protect the inner ear against overexposure (Brashears et al., 2003; Maison and Liberman, 2000). This raises the intriguing possibility that musical training might help strengthen the ear and actually protect against some forms of noise-related hearing damage. To our knowledge, the competing hypotheses of music as a catalyst vs. a deterrent to NIHL have not been fully tested.

A possible biological mechanism thought to protect the cochlea against acoustic trauma is the medial olivocochlear (MOC) efferent pathway (Patuzzi and Thompson, 1991). MOC neurons originate in the lower brainstem and terminate back in the auditory periphery where they innervate the cochlear outer hair cells. The role of the MOC efferents in human hearing is still debated. Nevertheless, several studies implicate this pathway in important aspects of real-world listening including (among other functions) playing an "antimasking" role (Bidelman and Bhagat, 2015; Guinan, 2006) to improve signal extraction in noise (Bidelman and Bhagat, 2015; Micheyl and Collet, 1996) and auditory learning (de Boer and Thornton, 2008). Additionally, given the MOC system is capable of regulating the gain of cochlear amplification (Guinan, 2006), it is also thought to play an important role in controlling input sound level and preventing acoustic damage to the ear (Kujawa and Liberman, 1997; Maison and Liberman, 2000). The critical importance of MOC feedback in protecting against acoustic vulnerability is evident in animal studies, which demonstrate that the integrity of this efferent fiber bundle is necessary to reduce temporary and permanent noise-induced threshold shifts (Kujawa and Liberman, 1997; Patuzzi and Thompson, 1991; Rajan, 1992; Zheng et al., 1997) and prevent synaptopathy (Maison et al., 2013) of the cochlear nerve fibers following traumatic acoustic exposure.

In humans, MOC activation can be assayed noninvasively via otoacoustic emissions (OAEs). OAEs are bioacoustic (cochlear emitted) sounds measured in the ear canal with highly sensitive microphones that reflect cochlear health and peripheral auditory processing (Kemp et al., 1990; Probst et al., 1991). Activation of the MOC bundle dampens outer hair cell electromotility through inhibition, resulting in measurable changes in cochlear emissions (Bhagat and Kilgore, 2014; Bidelman and Bhagat, 2015; Guinan, 2006; Philibert et al., 1998). Germane to our investigation, several lines of evidence suggest that MOC function might be sensitive to the experience-dependent effects of musicianship. Relative to their nonmusician peers, musically trained listeners experience less loudness adaptation (Micheyl et al., 1995) concurrent with a greater reduction in OAE amplitudes when sound is delivered to the contralateral ear (Brashears et al., 2003; Micheyl et al., 1995, 1997; Perrot et al., 1999)—both proxy measures of MOC activation. Moreover, we have recently shown that musicianship sharpens human cochlear tuning as assessed via OAE tuning curves (Bidelman et al., 2016). Presumably, these musician enhancements in cochlear processing could develop via enhanced MOC feedback, strengthened through protracted musical training and intensive interaction with complex auditory signals (Bidelman et al., 2016; Brashears et al., 2003; Micheyl et al., 1997).

Here, we extend this previous work to test the hypothesis that long-term music engagement can strengthen the temporal dynamics of ipsi- and contra-lateral MOC feedback to the ear. Experimental noise exposures are possible in animal studies (Maison et al., 2000), but is no longer ethically viable in human listeners given the potential risk of inducing permanent hearing loss (Maison et al., 2013). Thus, our general approach used a combination of perceptual and noninvasive physiological assays to measure hearing sensitivity and auditory function in musically trained (~10 years experience) and untrained listeners that are known to index acoustic vulnerability (Maison and Liberman, 2000). We estimated the strength of listeners' MOC efferent feedback in both the ipsilateral (crossed) and contralateral (uncrossed) olivocochlear pathways by measuring the adaptation time courses of distortion product (DP) OAEs (ipsilateral assay) and contralateral suppression (contralateral assay). OAE responses provide a non-invasive assay of cochlear health and are routinely used in audiological practice to detect noise-related impairments (Attias et al., 2001). Moreover, they serve as an early indicator of noise damage as changes in these cochlear responses precede the development of music-induced hearing deficits (Bhagat and Davis, 2008). Stronger ipsilateral and contralateral efferent cochlear gain control in musicians' OAEs would be consistent with the notion that musicianship might reduce noise vulnerability and overall susceptibility to acoustic trauma.

Upon energizing the cochlea, emissions typically adapt in amplitude over ~100–200 ms as neuronal MOC efferent feedback is engaged and cochlear amplification is attenuated (Backus and Guinan, 2006; Maison and Liberman, 2000; Warren and Liberman, 1989). Importantly, animal studies have shown that the magnitude of this DPOAE adaptation can be used to predict individual vulnerability to acoustic trauma (Maison and Liberman, 2000) and thus, a means to assess hearing risk. To date, this approach has only been successful in animal models (Maison and Liberman, 2000). By adapting this methodology for human application, we show that musicians have stronger MOC-related cochlear feedback than their nonmusician peers that varies with the length of their auditory training (i.e., experience-dependent manner). Our findings imply that musicianship might help reduce acoustic vulnerability to potentially damaging sounds by "toughening" the natural intensity regulation to the cochlea.

2. Materials & methods

2.1. Participants

Twenty young adults (age range: 18–31 years) participated in the experiment: 12 musicians (4 males, 8 females) and 8 nonmusicians (5 males, 3 females). Consistent with inclusion criteria and the definitions of "musician" and "nonmusician" used in previous reports (Bidelman et al., 2014a, 2016), musicians (Ms) were amateur instrumentalists who had received $\geq$ 9 years of continuous

formal instruction on their principal instrument ($\mu \pm SD$; 11.9 ± 3.2 yrs). Average onset age of musical instruction was 9.0 ± 1.5 yrs. Our musician cohort included a diverse set of backgrounds including woodwind (25%), brass players (25%), voice (8%), string (8%), and piano/percussion (33%) players. Nonmusicians (NMs) had ≤ 3 years of self-directed music training (0.8 ± 1.3yrs) and no instruction within the past five years.

All participants were native speakers of English, had normal audiometric thresholds (i.e., ≤20 dB HL at octave frequencies between 250 and 8000 Hz), normal middle ear function (i.e., Type-A tympanograms), and reported no previous history of neuropsychiatric illnesses. Critically, both groups were well-matched in hearing thresholds across the audiometric frequency range (all p-values > 0.41) (Fig. 1A). Previous studies have noted higher acoustic reflex thresholds (ART) in trained musicians, a measure of the middle ear muscle reflex (MEMR) (Brashears et al., 2003). However, we found no group differences in ARTs measured at 0.5, 1, 2, or 4 kHz (Fig. 1B). These controls rule out the possibility that any differences in DPOAE dynamics between musicians and nonmusicians arise due to trivial group differences in either hearing acuity or strength of the MEMR.

Aside from musical training, the two groups were otherwise closely matched in age (Ms: 23.0 ± 4.1 yrs, NMs: 23.3 ± 2.5 yrs; $t_{22} = -0.22$, $p = 0.83$), formal education (Ms: 17.5 ± 3.9 yrs, NMs: 16.2 ± 3.3 yrs; $t_{22} = 0.86$, $p = 0.40$) and right-handedness laterality index (Ms: 94.3 ± 12.5%, NMs: 89.2 ± 10.6%; $t_{22} = 1.03$, $p = 0.31$) (Oldfield, 1971). Participants were paid for their time and gave written informed consent in compliance with a protocol approved by the Institutional Review Board at the University of Memphis.

2.2. Otoacoustic emissions (OAEs)

The MOC efferent system is a bilateral reflex; sound delivered to one ear elicits both an ipsilateral and contralateral response (Gifford and Guinan, 1987; Smalt et al., 2014). Consequently, we measured and compared both ipsilateral and contralateral MOC efferent function between musicians and nonmusicians via adaptation time-courses (Maison and Liberman, 2000) and contralateral acoustic stimulation (CAS) (Bidelman and Bhagat, 2015; Guinan, 2006) of OAEs, respectively.

2.2.1. DPOAE recording procedure overview

For CAS recordings, DPOAEs were evoked by the simultaneous presentation of two primary tones (f_1 & f_2 with $f_2 > f_1$; $f_2/f_1 = 1.2$) to the right ear. The DPOAE was measured at the cubic difference tone frequency at $2f_1-f_2$ using primary tone levels of $L_1 = 60$ dB SPL and $L_2 = 50$ dB SPL (Zhang et al., 2007). Stimulus primaries were presented through a probe assembly containing miniature loud speakers and a microphone (Etymotic Research 10C). We varied the f_2 frequency at high resolution (1/50 octave increments) in the range from 1000 to 2000 Hz to measure the fine structure of DPOAE amplitude spectra. To be considered reliable responses, we required DPOAEs to have absolute amplitudes >−10 dB SPL and signal-to-noise ratios (SNRs) ≥ +6 dB. Signal averaging was terminated using measurement-based stopping rules (Mimosa Acoustics Hear ID). The stopping rules were as follows: The primary tone stimuli are presented and measurements are made in the ear canal in 1 s data frames. These data frames are averaged for a maximum duration of 10 s for each frequency point tested. The averaging process is terminated early if the stopping rule criteria are met. The joint criteria are twofold: (i) the noise floor level is averaged down to 0 dB SPL in the frequency bin of interest; (ii) DPOAE to noise floor SNR is at a minimum +10 dB. If these stopping criteria are not achieved in 10 s, the test frequency is changed and primary tone stimuli are presented/averaging at the new frequency begins. Artifact rejection was enabled and if the noise level was at 10 dB SPL or greater during a data frame, that frame was excluded from the averaged response.

2.2.2. Spontaneous emissions (SOAEs)

In addition to evoked OAEs, the ear can produce spontaneous otoacoustic emissions (SOAEs) recordable in the ear canal (Long, 1998). SOAEs can potentially influence the measurements of contralateral suppression of DPOAEs (Moulin et al., 1992) and could confound estimates of efferent function if measured proximal to an SOAE frequency. Therefore, prior to DPOAE recordings, we first screened listeners for spontaneous emissions using a synchronous recording approach (Sisto and Moleti, 1999). Sequences of clicks (inter-click interval = 40 ms) were presented at 50 dB peSPL. The number and frequency locations of SOAEs were identified during the silent intervals between clicks using an automated detection algorithm that identified SOAEs with a criterion SNR of +12 dB (Mimosa Acoustics Hear ID).

2.2.3. Contralateral acoustic stimulation (contralateral efferent feedback)

We first assessed the presence of MOC efferent activity in each group via contralateral acoustic stimulation (CAS) (Bidelman and

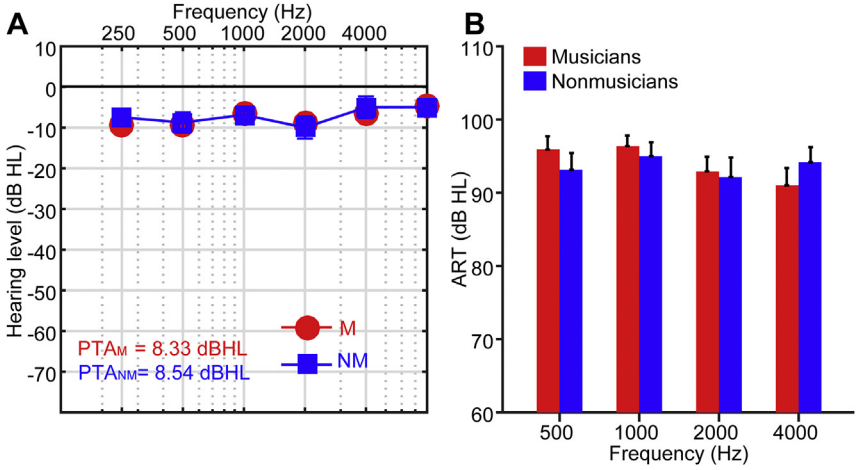

Fig. 1. Audiograms and acoustic reflex thresholds (ARTs) for musicians and nonmusicians. No group differences were observed in hearing thresholds nor ARTs (middle ear muscle activation) across the bandwidth of hearing. errorbars = ±1 s.e.m.

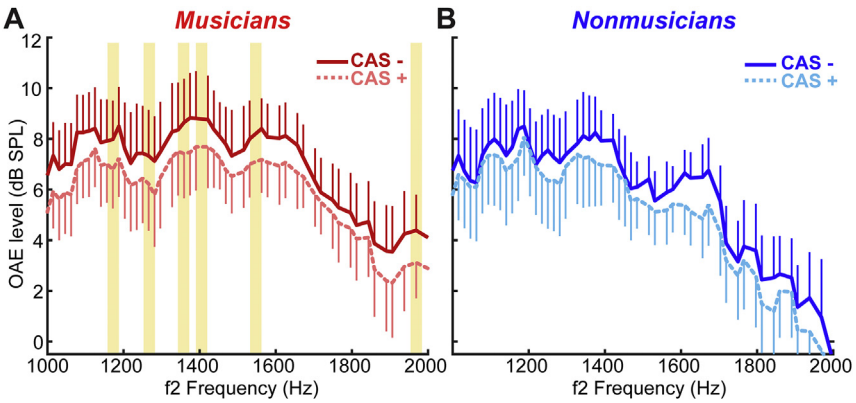

Fig. 2. Contralateral MOC reflexes are stronger in musicians. Shown here are DPOAE spectra for musicians (A) and nonmusicians (B) recorded in the right ear with (CAS+) and without (CAS-) the presence of noise in the left ear. Contralateral stimulation suppresses cochlear emissions, indicating activation of the MOC efferents and gain attenuation to the opposite cochlea. Shaded yellow areas demarcate frequencies with significant ($p < 0.05$) MOC suppression (i.e., CAS- > CAS + amplitudes) after FDR correction (Benjamini and Hochberg, 1995). Only musicians showed reliable contralateral MOC efferent feedback. Errorbars = ±1 s.e.m. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Bhagat, 2015). This technique has been applied previously to assess human efferent function and allowed us to replicate studies that have suggested stronger contralateral efferent activity in musicians (Brashears et al., 2003; Perrot et al., 1999). Noise presented to the contralateral ear attenuates OAEs recorded from the ipsilateral cochlea. Differences in emission levels between recordings made with (CAS+) and without (CAS-) contralateral noise stimulation provide a noninvasive index of contralateral MOC strength (Bidelman and Bhagat, 2015; Guinan, 2006). DPOAE response spectra were recorded with and without concurrent contralateral broadband noise (Brashears et al., 2003) (noise in left ear, OAE recorded in the right ear). We then compared the CAS+ and CAS- spectra for each group on a point-by-point frequency basis using a paired samples *t*-tests (two tailed). Frequencies showing significant MOC contralateral suppression (i.e., CAS- response > CAS+ response) were required to survive a significance level of $\alpha = 0.05$, corrected for multiple comparisons via false-discovery rate (FDR) (Benjamini and Hochberg, 1995).

In OAE recordings, there is often concern of involvement of the middle ear (i.e., MEMR) which can confound the measurements of emission amplitudes given the normal sound attenuating properties of this pathway (Gelfand, 2002). Consequently, the intensity of the contralateral noise was titrated for each listener to fall 10 dB lower than their contralateral MEMR threshold estimated via middle-ear power reflectance (Feeney and Keefe, 2001). Individual configuration of contralateral noise levels minimized the likelihood that DPOAE efferent suppression was due to inadvertent triggering the crossed MEMR (i.e., we ensured results would be of neural rather than muscular reflex origin).

2.2.4. MOC reflex strength assay (ipsilateral efferent feedback)

Human OAE (Berlin et al., 1995) and animal work (Gifford and Guinan, 1987; Smalt et al., 2014) suggests that the strength of the ipsilateral MOC reflex might be stronger than the contralateral reflex, as much as a factor of ~2:1 (but see Lilaonitkul and Guinan, 2012). Consequently, ipsilateral MOC strength is likely to provide a more sensitive measure of cochlear gain modulation and hence, potential acoustic risk (Maison and Liberman, 2000). To estimate ipsilateral MOC reflex strength, we measured post-onset adaptation of the DPOAE time course (Liberman et al., 1996; Maison et al., 2000). In normal ears, the amplitude of the DP frequency ($2f_1-f_2$) measured from an emission adapts rapidly after the initiation of the two stimulus primaries, decaying exponentially to a steady-state response over the course of ~100 ms (e.g., see Fig. 3A). The time constant of this adaptation is consistent with measures of olivocochlear function (Backus and Guinan, 2006; Warren and Liberman, 1989) as evident by its eradication following efferent ablation (Liberman et al., 1996). Post-stimulus adaptation of the DPOAE is thought to reflect activation of the efferent MOC pathway and consequently, a decrement in OHC motility and cochlear amplification (Maison and Liberman, 2000). As such, the magnitude of OAE adaptation provides a proxy measure of (ipsilateral) MOC reflex strength.

DPOAEs were measured using 512 ms primary tones, presented at a rate of 1/sec. DPOAE time courses were then computed from the running FFT (50 ms sliding window, 5-ms steps) applied to response time waveforms recorded in the right ear (without inclusion of noise). For each listener, time-varying amplitudes were extracted across consecutive windows at the Fourier bin corresponding to the DP frequency (i.e., $2f_1-f_2$) that produced maximum amplitude in their DPOAE fine structure, where efferent-induced changes are most prominent (Abdala et al., 2009). We also ensured this frequency was spectrally remote (>±50 Hz) from any activity identified in listeners' spontaneous SOAE emissions. Following animal studies (Maison and Liberman, 2000), we defined MOC reflex strength as the difference in dB between the DP emission amplitude at stimulus onset and its final steady-state value, where the latter was defined as the mean of the last five time points along the response trace. This provided an estimate of the MOC activation strength (termed "MOC effect") for each combination of primary levels. Five to eight primary-tone level combinations were used, resulting in $|L_1-L_2|$ level differences ranging from 0 to 26 dB (Maison and Liberman, 2000). As observed in animal recordings (Maison and Liberman, 2000), this post-stimulus adaptation magnitude was either negative, positive, or invariant depending on the differential in L_1-L_2 intensity (see Fig. 3C). To estimate a singular value of each listener's overall MOC reflex strength, we calculated the difference between the maximum and minimum of their level-dependent effect function (i.e., Fig. 4) (Maison and Liberman, 2000). This max-min metric was computed for each listener and allowed us to compare (ipsilateral) MOC reflex strength between musician and nonmusician listeners.

3. Results

3.1. Contralateral efferent strength

Group estimates of contralateral MOC function measured via

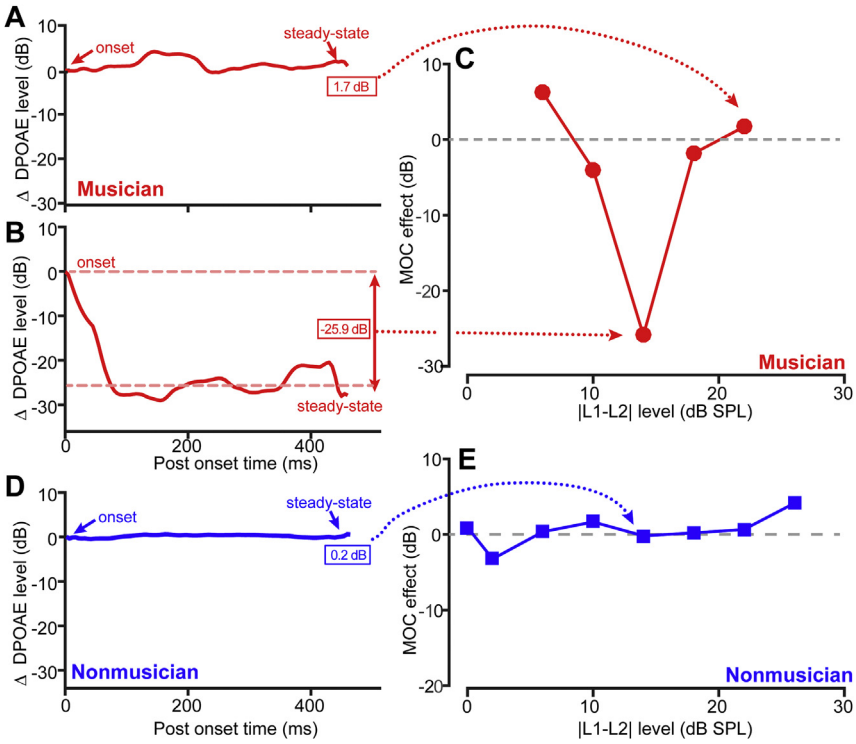

Fig. 3. Ipsilateral post-stimulus adaptation of DPOAE amplitudes provides a proxy of MOC reflex strength and is stronger in musicians. (A–C) Data from a representative musician ear illustrating a strong reflex. (D–E) Data from a nonmusician with weak reflex. A, B, and D show raw data for specific primary tone level combination. Certain levels produce little adaption of the DPOAE time course (e.g., A, D) whereas others yield a decay toward a steady-state response over ~100 ms (B), particularly in musically trained ears. C and E show the magnitude (and sign) of the adaptation effect across different stimulus level combinations (see Fig. 4 for all individual data by group). Overall, musicians show larger magnitudes than nonmusicians representing a stronger MOC reflex strength.

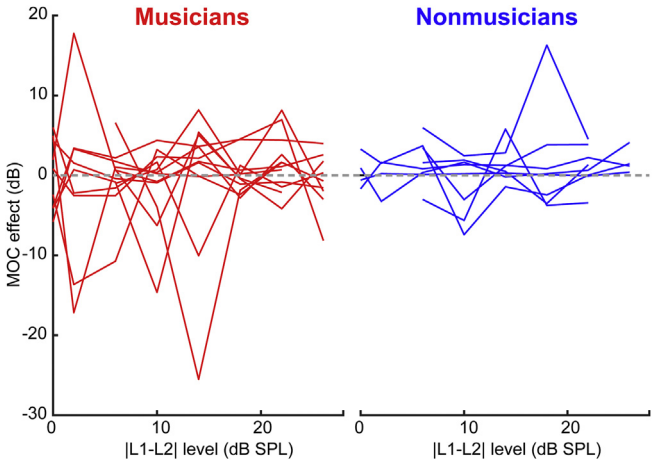

Fig. 4. Individual MOC-level effect functions. Otherwise as in Fig. 3 C and E. MOC reflex strength (i.e., Fig. 5A) was measured as the difference between the maximum and minimum points of these level-dependent MOC functions. Note the larger excursion of effect in musicians compared to nonmusicians, reflecting larger modulations in the strength of their MOC reflex.

CAS are shown in Fig. 2. In both groups, cochlear emission spectra appeared weaker with noise delivered to the opposite ear (CAS+) than when recorded in quiet (CAS-). However, only musicians showed reliable ($p_{FDR} < 0.05$) MOC-induced contralateral suppression after correcting for multiple comparisons. Musicians' MOC suppression effects were most evident in the 1000–1500 Hz region. These findings replicate and confirm previous studies demonstrating stronger contralateral efferent control in musicians (Brashears et al., 2003; Perrot and Collet, 2014; Perrot et al., 1999). Averaged across the frequency spectrum, we did not find a significant correlation between the CAS efferent effect (i.e., difference between CAS- and CAS+, in dB) and listeners' years of musical training ($r = 0.12$, $p = 0.59$; data not shown).

3.2. Ipsilateral efferent strength

Ipsilateral MOC feedback has not yet been assessed for experience-dependent plasticity (cf. Perrot and Collet, 2014). In ipsilateral recordings, presentation of the f_1 and f_2 stimulus primaries resulted in a cochlear emission at the DPOAE frequency (i.e., $2f_1–f_2$) whose amplitude adapted over the ~100–200 post stimulus onset. A comparison of DPOAE adaptation time courses for a representative musician and nonmusician listener are shown in Fig. 3A–E. Depending on the specific difference between $L_1–L_2$ intensity, DPOAE amplitude either decayed to steady-state, increased, or remained invariant across the 500 ms recording epoch window. The magnitude of this post-stimulus adaptation is shown for the various level combinations in Fig. 3C and E for a representative musician and nonmusician, respectively, whereas group data are shown in Fig. 4. At certain level combinations, musicians showed stronger DPOAE adaptation than their nonmusician peers, despite having similar audiometric thresholds, ARTs (i.e., middle ear function), and the identical eliciting stimulus (cf. Fig. 3C and E). In contrast, nonmusicians showed little to no adaptation across the majority of stimulus level combinations (individual subject comparisons: Fig. 3D–E; group comparison: Fig. 4). For each listener per group, a measure of aggregate (ipsilateral) MOC reflex strength was taken as the difference between the maximum and minimum points of their level-dependent MOC

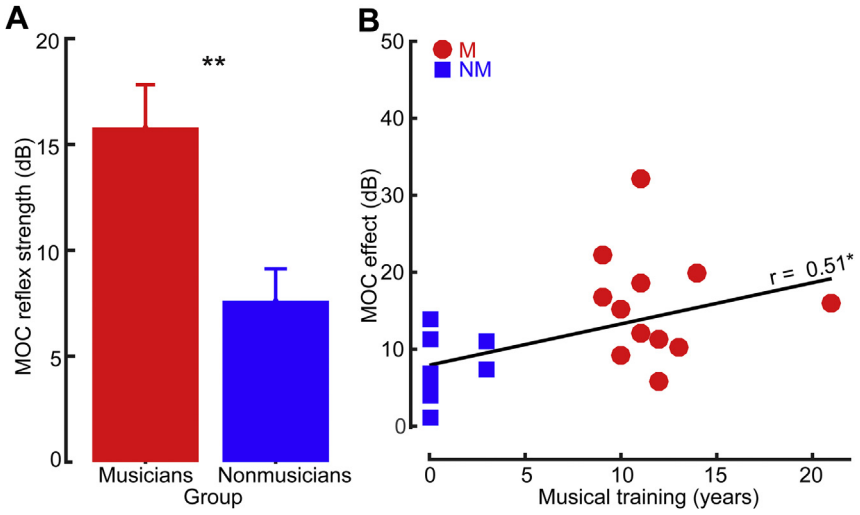

Fig. 5. MOC reflex is stronger in musicians and is experience-dependent. (A) MOC reflex strength is ~2× stronger in musically trained ears relative to musically naïve listeners. (B) Strength of the MOC effect is positively correlated with listeners' years of formal musical training such that more extensive listening experience predicts stronger MOC reflex strength. $^{*}p < 0.05$, $^{**}p < 0.01$, errorbars = ±1 s.e.m.

function (i.e., Fig. 4).

On average, ipsilateral MOC reflex strength was +8.1 dB stronger in musically trained ears relative to musically naïve listeners (Fig. 5A) [$t_{18} = 2.95$, $p = 0.0086$].[1] Importantly, the MOC effect showed no correspondence with ARTs for either group (Pearson-*r*: $r_M = 0.34$, $p = 0.28$; $r_{NM} = 0.31$, $p = 0.44$), making it unlikely that the MEMR was a major contributor to the measurements. This helps further confirm that OAE effects were attributed to MOC efferent gain control (i.e., neuronal function) (Liberman et al., 1996) rather than trivial differences in hearing acuity or middle ear MEMR function. Interestingly, correlational analyses revealed a positive association between listeners' years of formal music training and the strength of the physiological MOC effect when considering musical training as a continuous variable regardless of groups ($r = 0.51$, $p = 0.022$; Fig. 5B). Longer extents of music engagement predicted stronger MOC activation. These findings reveal stronger MOC efferent feedback in musically trained ears that depends on the length of their listening experience. Correlations by group were not significant ($r_M = -0.07$, $p = 0.80$; $r_{NM} = 0.30$, $p = 0.60$).

We also evaluated the relation between ipsilateral and contralateral MOC strength. However, we found no reliable association between these measures ($r = -0.03$, $p = 0.91$).

4. Discussion

By measuring the temporal dynamics of cochlear emissions (DPOAEs) in classically trained musicians and nonmusicians, our findings reveal that on average, trained listeners have stronger sound-evoked neuronal feedback to the cochlea than their nonmusician peers, produced by enhanced modulatory gain control in both the ipsi- and contra-lateral arc of the olivocochlear system (i.e., brainstem→cochlear efferents). Moreover, this efferent enhancement varies with the extent of listeners' musical training, such that longer music engagement is linked to stronger MOC feedback. Musicians' stronger MOC reflexes were observed in the absence of group differences in audiometric or acoustic reflex thresholds, indicating that the observed effects were not due to differences in hearing sensitivity or middle ear physiology, but rather efferent neuronal function. Our findings bolster the notion that rigorous auditory experiences can enhance even the most peripheral stages of the auditory system well before neocortical structures (Bidelman et al., 2014a, 2016).

In animal models, MOC reflex strength—estimated via the DPOAE adaptation approach used here—has been interpreted as a noninvasive measure of vulnerability to acoustic injury, i.e., distinguishing "tender" vs. "tough" ears (Maison and Liberman, 2000). Indeed, using identical methodology in guinea pigs (Maison and Liberman, 2000), previous studies have shown that animals with stronger MOC reflexes ("tough" ears) are less likely to acquire permanent hearing loss after subsequent damaging noise exposure. In so much as OAE-derived MOC strength similarly reflects acoustic vulnerability in *humans*, our findings imply that protracted musical training might help reduce acoustic vulnerability to potentially damaging sounds by "toughening" the natural intensity regulation to the cochlea.

Some studies suggest that musicians might have stronger MEMR thresholds, as measured via ARTs (Brashears et al., 2003). Although we found no group differences in ARTs in the current study, it is also possible that musicians might be able to anticipate louder portions of incoming sound (e.g., in a learned musical piece) and volitionally increase MEMR before the occurrence of louder passages. Volitional control of MEMR could offer another possible protective strategy for musicians but has yet to be validated empirically. Future studies are needed to test this hypothesis.

Evidence that musicianship is either a catalyst or deterrent to noise-induced hearing loss has been equivocal. Some studies report increased noise risk in classical musicians (Henning and Bobholz, 2016; Jansen et al., 2009; Otsuka et al., 2016; Phillips et al., 2010; Toppila et al., 2011), while others report only individual cases of hearing loss, with the majority of sampled musicians show normal or better hearing (present study; Karlsson et al., 1983; Reuter and Hammershoi, 2007; Russo et al., 2013; Schmidt et al., 2014). Variation between sample demographics aside, our data here are more consistent with the latter findings. We did not observe any

[1] DP frequency locations were higher on average in musicians compared to nonmusicians [M: 930 ± 144 Hz, NM: 780 ± 78 Hz; $t_{18} = 2.66$, $p = 0.016$]. However, this difference was minimal (~150 Hz = 0.25 octaves) which is smaller than amplitude "ripple" spacing (0.33 oct) effects observed in DPOAE spectral fine structure (Reuter and Hammershoi, 2006). Moreover, it should be emphasized that the MOC adaptation measured here is a *relative* measure (time-varying amplitude *re*. onset), and is not dependent on absolute levels of the emission. More critically, DP frequency was not associated with MOC reflex strength in either group ($r_M = 0.13$, $p = 0.69$; $r_{NM} = 0.01$, $p = 0.97$), suggesting an independence of these measures.

differences between trained and untrained listeners in terms of conventional audiological tests, confirming normal and equivalent hearing thresholds (up to 8 kHz) and middle ear function. These findings corroborate previous studies where systematic measures of noise dosage and audiometric hearing have suggested better hearing in professional orchestral musicians than expected for their age (Obeling and Poulsen, 1999; Schmidt et al., 2014). Interestingly, classical musicians who are chronically exposed to moderate noise levels (i.e., 90–95 dBA) for several decades similarly demonstrate better hearing acuity than expected from their total noise-exposure history according to international standards (ISO 1999, 1990; Obeling and Poulsen, 1999). Other studies that have monitored hearing longitudinally (>6 years), have found no increased risk of hearing damage in musicians above and beyond normal age-related changes in threshold acuity (Karlsson et al., 1983). While musicianship certainly cannot prevent all hearing losses (e.g., age-related presbycusis), these previous studies coupled with our current findings are at least suggestive that intense auditory experiences might help strengthen the hearing mechanism and possibly offset its negative effects on some aspects of hearing function (e.g., Bidelman and Alain, 2015; Parbery-Clark et al., 2012; Zendel and Alain, 2012).

Our cohort was limited to classically trained musicians. Future studies are needed to determine if our findings hold for other genres of music, particularly instrumentalists who are undoubtedly exposed to much higher sound levels (e.g., rock or jazz players). Elevated thresholds in musicians, when observed, are typically reported for frequencies >2–3 kHz (Russo et al., 2013; Toppila et al., 2011) and with higher shifts in brass players and percussionists (Russo et al., 2013). Thus, it remains possible that MOC enhancement effects observed here in the 1–2 kHz region might diminish at higher frequencies more vulnerable to music-related NIHL. Additionally, it would be interesting to assess whether or not these findings hold, for instance, in older musicians, who would have had both more cumulative years of loud sound exposure and greater vulnerability due to aging. If our hypothesis is correct, the difference between older musicians' and nonmusicians' MOC function may be even greater than observed here; while the musically naïve ear might show normal age-related degradations from life-long noise exposure, those of musicians might be protected. Along these lines, there is some evidence to suggest that older musicians experience *less* age-related decline in neural and behavioral sound processing, particularly those related to complex (e.g., speech) listening skills (Bidelman and Alain, 2015; Parbery-Clark et al., 2012; Zendel and Alain, 2012).

Ideally, validation of hearing loss risk would have required that we evaluate changes in hearing status in musicians and nonmusicians before and after controlled noise exposure (e.g., Pirila, 1991; Ward, 1970). While experimental noise exposure is possible in animal studies (Maison et al., 2000), this approach is no longer ethically viable in human listeners given the potential risk of inducing permanent hearing loss with even moderate (i.e., ~85 dBA) levels of exposure (Maison et al., 2013). Consequently, while the OAE/MOC indices used here are widely accepted physiological assays of cochlear health and acoustic vulnerability (Attias et al., 2001; Kemp et al., 1990; Maison and Liberman, 2000; Otsuka et al., 2016; Probst et al., 1991), our data assume that these responses would predict listeners' propensity to acquire hearing loss after an actual overexposure. Ethical considerations preclude explicit testing of this hypothesis. Although, assessment of OAE/MOC responses before and after the noise exposure of a rehearsal could be a comprising approach (Otsuka et al., 2016). Nevertheless, there are several lines of indirect evidence to suggest that musicians' stronger MOC efferent function we observe here would indeed protect against acoustic trauma.

In animal models, sectioning the MOC efferent pathway abolishes its protective effect against acoustic trauma (Patuzzi and Thompson, 1991). Interestingly, normal intersubject variability in noise vulnerability (Cody and Robertson, 1983; Patuzzi and Thompson, 1991) is also dramatically reduced following lesioning of this pathway (Patuzzi and Thompson, 1991). A drop in variability after efferent sectioning suggests that individual differences in noise trauma susceptibility might be attributed to differing tonic activation and/or sensitivity of the olivocochlear system (Patuzzi and Thompson, 1991). Our data here reveal that a person's listening experience is one possible mechanism that can produce individual differences in human olivocochlear function and potential acoustic vulnerability.

In this vein, correlational analysis showed an association between the years of listeners' musical training and ipsilateral MOC feedback, though correlations by group did not reach significance (Fig. 4B). This latter finding could reflect the fact that musicians of our study had relatively homogenous levels of musical training (~5–8 years), precluding within-group correlations. Actively, another hypothesis consistent with these data is that 5–8 years of musical training is required to boost the MOC reflex and that more training does not necessarily provide any additional benefit. That is, experience-dependent MOC enhancements are fully engaged by five years of musical training. Corroborating this notion, recent studies examining brainstem potentials suggest that enhancement in subcortical auditory processing with musicianship are retained into adulthood, even when music lessons are interrupted in adolescence (Skoe and Kraus, 2012; White-Schwoch et al., 2013).

Our results provide new evidence that musicians have “tougher” ears as evident by stronger ipsi/contralateral MOC feedback and cochlear gain control. Moreover, we find these effects are experience-dependent as they covary with the years of individual's musical training. Presumably, enduring moderate (but non-damaging) sound levels during music engagement could strengthen tonic MOC activation over time to further sensitize olivocochlear efferent function (e.g., Bidelman et al., 2016). Under this interpretation, sound levels experienced during repeated music rehearsal might tone MOC function over longer time courses, akin to the effects of physical fitness on muscle strength (Kraus and Chandrasekaran, 2010). Interestingly, musicianship has been shown to offset certain age-related declines in auditory processing (Bidelman and Alain, 2015; Zendel and Alain, 2012). Moreover, recent animal work reveals that stronger MOC feedback can slow age-related changes in auditory function (Liberman et al., 2014). Assimilating these findings, it is provocative to think that at least some of older musicians' listening benefits (Bidelman and Alain, 2015; Parbery-Clark et al., 2012; Zendel and Alain, 2012) might be accounted for by enhanced MOC feedback and a “toughening” of the peripheral input as observed here.

While our data do not allow us to extrapolate the observed effects to other listening experiences, it would be worthwhile to examine if other forms of moderate acoustic exposures can similarly strengthen MOC function and protective mechanisms of hearing (e.g., in users of personal music players who regularly listen at moderate but unharmful levels). Presently, a reliable method to predict human susceptibility to noise damage has not been identified (Melnick, 1991). More broadly, the MOC measures employed here could be adopted to assess acoustic risk and monitor hearing loss in musicians (Otsuka et al., 2016) and other types of occupational noise environments.

Author contributions

G.M.B. and S.P.B. designed the experiment, A.D.S. and V.R.H. collected the data, A.D.S. and G.M.B. analyzed the data, and G.M.B.

and S.P.B. wrote the paper.

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References

Abdala, C., Mishra, S.K., Williams, T.L., 2009. Considering distortion product otoacoustic emission fine structure in measurements of the medial olivocochlear reflex. J. Acoust. Soc. Am. 125, 316–325.
Alain, C., Zendel, B.R., Hutka, S., Bidelman, G.M., 2014. Turning down the noise: the benefit of musical training on the aging auditory brain. Hear. Res. 308, 162–173.
Attias, J., Horovitz, G., El-Hatib, N., Nageris, B., 2001. Detection and clinical diagnosis of noise-induced hearing loss by otoacoustic emissions. Noise Health 3, 19–31.
Backus, B.C., Guinan Jr., J.J., 2006. Time-course of the human medial olivocochlear reflex. J. Acoust. Soc. Am. 119, 2889–2904.
Benjamini, Y., Hochberg, Y., 1995. Controlling the false discovery rate: a practical and powerful approach to multiple testing. Journal of the Royal Statistical Society. Ser. B Methodol. 57, 289–300.
Berlin, C.I., Hood, L.J., Hurley, A.E., Wen, H., Kemp, D.T., 1995. Binaural noise suppresses linear click-evoked otoacoustic emissions more than ipsilateral or contralateral noise. Hear. Res. 87, 96–103.
Bhagat, S.P., Davis, A.M., 2008. Modification of otoacoustic emissions following ear-level exposure to MP3 player music. Int. J. Audiol. 47, 751–760.
Bhagat, S.P., Kilgore, C., 2014. Efferent-mediated reduction in cochlear gain does not alter tuning estimates from stimulus-frequency otoacoustic emission group delays. Neurosci. Lett. 559, 132–135.
Bidelman, G.M., 2016. Musicians have enhanced audiovisual multisensory binding: experience-dependent effects in the double-flash illusion. Exp. Brain Res. 234, 3037–3047.
Bidelman, G.M., Bhagat, S.P., 2015. Right ear advantage drives the link between olivocochlear efferent "antimasking" and speech-in-noise listening benefits. NeuroReport 26, 483–487.
Bidelman, G.M., Alain, C., 2015. Musical training orchestrates coordinated neuroplasticity in auditory brainstem and cortex to counteract age-related declines in categorical vowel perception. J. Neurosci. 35, 1240–1249.
Bidelman, G.M., Gandour, J.T., Krishnan, A., 2011. Cross-domain effects of music and language experience on the representation of pitch in the human auditory brainstem. J. Cogn. Neurosci. 23, 425–434.
Bidelman, G.M., Nelms, C., Bhagat, S.P., 2016. Musical experience sharpens human cochlear tuning. Hear. Res. 335, 40–46.
Bidelman, G.M., Schug, J.M., Jennings, S.G., Bhagat, S.P., 2014a. Psychophysical auditory filter estimates reveal sharper cochlear tuning in musicians. J. Acoust. Soc. Am. 136, EL33–EL39.
Bidelman, G.M., Weiss, M.W., Moreno, S., Alain, C., 2014b. Coordinated plasticity in brainstem and auditory cortex contributes to enhanced categorical speech perception in musicians. Eur. J. Neurosci. 40, 2662–2673.
Brashears, S.M., Morlet, T.G., Berlin, C.I., Hood, L.J., 2003. Olivocochlear efferent suppression in classical musicians. J. Am. Acad. Audiol. 14, 314–324.
Cody, A.R., Robertson, D., 1983. Variability of noise-induced damage in the Guinea pig cochlea: electrophysiological and morphological correlates after strictly controlled exposures. Hear. Res. 9, 55–70.
de Boer, J., Thornton, A.R., 2008. Neural correlates of perceptual learning in the auditory brainstem: efferent activity predicts and reflects improvement at a speech-in-noise discrimination task. J. Neurosci. 28, 4929–4937.
Feeney, M.P., Keefe, D.H., 2001. Estimating the acoustic reflex threshold from wideband measures of reflectance, admittance, and power. Ear Hear 22, 316–332.
Gelfand, S.A., 2002. The acoustic reflex. In: Katz, J. (Ed.), Handbook of Clinical Audiology, fifth ed. Lippincott Williams & Wilkins, Baltimore, MD, pp. 205–232.
Gifford, M.L., Guinan Jr., J.J., 1987. Effects of electrical stimulation of medial olivocochlear neurons on ipsilateral and contralateral cochlear responses. Hear. Res. 29, 179–194.
Gopal, K.V., Chesky, K., Beschoner, E.A., Nelson, P.D., Stewart, B.J., 2013. Auditory risk assessment of college music students in jazz band-based instructional activity. Noise Health 15, 246–252.
Guinan Jr., J.J., 2006. Olivocochlear efferents: anatomy, physiology, function, and the measurement of efferent effects in humans. Ear Hear 27, 589–607.
Henning, R.L., Bobholz, K., 2016. Distortion product otoacoustic emissions in college music majors and nonmusic majors. Noise Health 18, 10–20.
Herholz, S.C., Zatorre, R.J., 2012. Musical training as a framework for brain plasticity: behavior, function, and structure. Neuron 76, 486–502.
ISO1999, 1990. Acoustics—determination of Occupational Noise Exposure and Estimation of Noise-induced Hearing Impairment. International Organization for Standardization, Geneva, Switzerland.
Jansen, E.J., Helleman, H.W., Dreschler, W.A., et al., 2009. Noise induced hearing loss and other hearing complaints among musicians of symphony orchestras. Int. Arch. Occup. Environ. Health 82, 153–164.
Karlsson, K., Lundquist, P.G., Olaussen, T., 1983. The hearing of symphony orchestra musicians. Scand. Audiol. 12, 257–264.
Kemp, D.T., Ryan, S., Bray, P., 1990. A guide to the effective use of otoacoustic emissions. Ear Hear 11, 93–105.
Kraus, N., Chandrasekaran, B., 2010. Music training for the development of auditory skills. Nat. Rev. Neurosci. 11, 599–605.
Kujawa, S.G., Liberman, M.C., 1997. Conditioning-related protection from acoustic injury: effects of chronic deefferentation and sham surgery. J. Neurophysiol. 78, 3095–3106.
Levey, S., Fligor, B.J., Ginocchi, C., Kagimbi, L., 2012. The effects of noise-induced hearing loss on children and young adults. Contemp. Issues Commun. Sci. Disord. 39, 76–83.
Liberman, M.C., Puria, S., Guinan, J.J., 1996. The ipsilaterally evoked olivocochlear reflex causes rapid adaptation of the 2f1−f2 DPOAE. J. Acoust. Soc. Am. 99, 3572–3584.
Liberman, M.C., Liberman, L.D., Maison, S.F., 2014. Efferent feedback slows cochlear aging. J. Neurosci. 34, 4599–4607.
Lilaonitkul, W., Guinan Jr., J.J., 2012. Frequency tuning of medial-olivocochlear-efferent acoustic reflexes in humans as functions of probe frequency. J. Neurophysiol. 107, 1598–1611.
Long, G., 1998. Perceptual consequences of the interactions between spontaneous otoacoustic emissions and external tones. I. Monaural diplacusis and aftertones. Hear. Res. 119, 49–60.
Maison, S., Micheyl, C., Andéol, G., Gallégo, S., Collet, L., 2000. Activation of medial olivocochlear efferent system in humans: influence of stimulus bandwidth. Hear. Res. 140, 111–125.
Maison, S.F., Liberman, M.C., 2000. Predicting vulnerability to acoustic injury with a noninvasive assay of olivocochlear reflex strength. J. Neurosci. 20, 4701–4707.
Maison, S.F., Usubuchi, H., Liberman, M.C., 2013. Efferent feedback minimizes cochlear neuropathy from moderate noise exposure. J. Neurosci. 33, 5542–5552.
Melnick, W., 1991. Human temporary threshold shift (TTS) and damage risk. J. Acoust. Soc. Am. 90, 147–154.
Micheyl, C., Collet, L., 1996. Involvement of the olivocochlear bundle in the detection of tones in noise. J. Acoust. Soc. Am. 99, 1604–1610.
Micheyl, C., Carbonnel, O., Collet, L., 1995. Medial olivocochlear system and loudness adaptation: differences between musicians and non-musicians. Brain Cogn. 29, 127–136.
Micheyl, C., Khalfa, S., Perrot, X., Collet, L., 1997. Difference in cochlear efferent activity between musicians and non-musicians. Neuroreport 8, 1047–1050.
Møllerløkken, O.J., Magerøy, N., Bråtveit, M., Lind, O., Moen, B.E., 2013. Forte fortissimo for amateur musicians: No effect on otoacoustic emissions. Med. Probl. Perform. Art. 28, 3–8.
Moreno, S., Bidelman, G.M., 2014. Understanding neural plasticity and cognitive benefit through the unique lens of musical training. Hear. Res. 308, 84–97.
Moulin, A., Collet, L., Morgon, A., 1992. Influence of spontaneous otoacoustic emission (SOAE) on acoustic distortion product input/output functions: does the medial efferent system act differently in the vicinity of an SOAE? Acta Otolaryngol. 112, 210–214.
Musacchia, G., Sams, M., Skoe, E., Kraus, N., 2007. Musicians have enhanced subcortical auditory and audiovisual processing of speech and music. Proc. Natl. Acad. Sci. U. S. A. 104, 15894–15898.
NIH/NIDCD, 2008. Noise-induced Hearing Loss [Online] (verified Sept. 15, 2013). http://www.nidcd.nih.gov/health/hearing/pages/noise.aspx.
NIOSH, 1998. Criteria for a Recommended Standard: Occupational Noise Exposure (DHHS Publication No. 98–126). National Institute for Occupational Safety and Health, Atlanta, GA. Available from: http://www.cdc.gov/niosh/docs/98-126/.
Obeling, L., Poulsen, T., 1999. Hearing ability in Danish symphony orchestra musicians. Noise Health 1, 43–49.
Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9, 97–113.
Otsuka, S., Tsuzaki, M., Sonoda, J., Tanaka, S., Furukawa, S., 2016. A role of medial olivocochlear reflex as a protection mechanism from noise-induced hearing loss revealed in short-practicing violinists. PLoS One 11, e0146751.
Parbery-Clark, A., Anderson, S., Hittner, E., Kraus, N., 2012. Musical experience offsets age-related delays in neural timing. Neurobiol. Aging 33 (1483), e1–4.
Patuzzi, R.B., Thompson, M.L., 1991. Cochlear efferent neurones and protection against acoustic trauma: protection of outer hair cell receptor current and interanimal variability. Hear. Res. 54, 45–58.
Perrot, X., Collet, L., 2014. Function and plasticity of the medial olivocochlear system in musicians: a review. Hear. Res. 308, 27–40.
Perrot, X., Micheyl, C., Khalfa, S., Collet, L., 1999. Stronger bilateral efferent influences on cochlear biomechanical activity in musicians than in non-musicians. Neurosci. Lett. 262, 167–170.
Philibert, B., Veuillet, E., Collet, L., 1998. Functional asymmetries of crossed and uncrossed medial olivocochlear efferent pathways in humans. Neurosci. Lett. 253, 99–102.
Phillips, S.L., Henrich, V.C., Mace, S.T., 2010. Prevalence of noise-induced hearing loss in student musicians. Int. J. Audiol. 49, 309–316.
Pirila, T., 1991. Left-right asymmetry in the human response to experimental noise exposure. II. Pre-exposure hearing threshold and temporary threshold shift at 4 kHz frequency. Acta Otolaryngol. 111, 861–866.
Poissant, S.F., Freyman, R.L., MacDonald, A.J., Nunes, H.A., 2012. Characteristics of noise exposure during solitary trumpet playing: immediate impact on distortion-product otoacoustic emissions and long-term implications for hearing. Ear Hear 33, 543–553.
Probst, R., Lonsbury-Martin, B.L., Martin, G.K., 1991. A review of otoacoustic

emissions. J. Acoust. Soc. Am. 89, 2027–2067.
Rabinowitz, P.M., 2000. Noise-induced hearing loss. Am. Fam. Physician 61, 2749–2756.
Rajan, R., 1992. Protective functions of the efferent pathways to the mammalian cochlea: a review. In: Dancer, A.L., Henderson, D., Salvi, R.J., Hamernik, R.P. (Eds.), Noise-induced Hearing Loss. Mosby Year Book, St. Louis, pp. 429–444.
Reuter, K., Hammershoi, D., 2006. Distortion product otoacoustic emission fine structure analysis of 50 normal-hearing humans. J. Acoust. Soc. Am. 120, 270–279.
Reuter, K., Hammershoi, D., 2007. Distortion product otoacoustic emission of symphony orchestra musicians before and after rehearsal. J. Acoust. Soc. Am. 121, 327–336.
Royster, J.D., R, L.H., Killion, M.C., 1991. Sound exposures and hearing thresholds of symphony orchestra musicians. J. Acoust. Soc. Am. 89, 2793–2803.
Russo, F.A., Behar, A., Chasin, M., Mosher, S., 2013. Noise exposure and hearing loss in classical orchestra musicians. Int. J. Ind. Ergon. 43, 474–478.
Schmidt, J.H., Pedersen, E.R., Juhl, P.M., et al., 2011. Sound exposure of symphony orchestra musicians. Ann. Occup. Hyg. 55, 893–905.
Schmidt, J.H., Pedersen, E.R., Paarup, H.M., Christensen-Dalsgaard, J., Andersen, T., Poulsen, T., Baelum, J., 2014. Hearing loss in relation to sound exposure of professional symphony orchestra musicians. Ear Hear 35, 448–460.
Schneider, P., Scherg, M., Dosch, H.G., Specht, H.J., Gutschalk, A., Rupp, A., 2002. Morphology of Heschl's gyrus reflects enhanced activation in the auditory cortex of musicians. Nat. Neurosci. 5, 688–694.
Shahin, A., Bosnyak, D.J., Trainor, L.J., Roberts, L.E., 2003. Enhancement of neuroplastic P2 and N1c auditory evoked potentials in musicians. J. Neurosci. 23, 5545–5552.
Sisto, R., Moleti, A., 1999. Modeling otoacoustic emissions by active nonlinear oscillators. J. Acoust. Soc. Am. 106, 1893–1906.
Skoe, E., Kraus, N., 2012. A little goes a long way: how the adult brain is shaped by musical training in childhood. J. Neurosci. 32, 11507–11510.
Smalt, C.J., Heinz, M.G., Strickland, E.A., 2014. Modeling the time-varying and level-dependent effects of the medial olivocochlear reflex in auditory nerve responses. J. Assoc. Res. Oto 15, 159–173.
Strait, D.L., Kraus, N., 2014. Biological impact of auditory expertise across the life span: musicians as a model of auditory learning. Hear. Res. 308, 109–121.
Toppila, E., Koskinen, H., Pyykkö, I., 2011. Hearing loss among classical-orchestra musicians. Noise Health 13, 45–50.
USDoVA, U.S.D.o.V.A, 2005. Veterans Benefit Administration Reports Home [Internet]. United States Department of Veterans Affairs; 2009. Annual benefits reports FY 2005. Washington, DC. http://www.vba.va.gov/REPORTS/abr/historical/2005_abr.pdf.
Ward, W.D., 1965. The concept of susceptibility to hearing loss. J. Occup. Med. 7, 595–607.
Ward, W.D., 1970. Temporary threshold shift and damage-risk criteria for intermittent noise exposures. J. Acoust. Soc. Am. 48, 561–574.
Warren, E.H., Liberman, M.C., 1989. Effects of contralateral sound on auditory-nerve responses. I. Contributions of cochlear efferents. Hear. Res. 37, 89–104.
White-Schwoch, T., Carr, K.W., Anderson, S., Strait, D.L., Kraus, N., 2013. Older adults benefit from music training early in life: biological evidence for long-term training-driven plasticity. J. Neurosci. 33, 17667–17674.
WHO, 2015. Hearing Loss Due to Recreational Exposure to Loud Sounds: A Review. World Health Organization. http://apps.who.int/iris/bitstream/10665/154589/1/9789241508513_eng.pdf.
Wong, P.C., Skoe, E., Russo, N.M., Dees, T., Kraus, N., 2007. Musical experience shapes human brainstem encoding of linguistic pitch patterns. Nat. Neurosci. 10, 420–422.
Zatorre, R., McGill, J., 2005. Music, the food of neuroscience? Nature 434, 312–315.
Zendel, B.R., Alain, C., 2012. Musicians experience less age-related decline in central auditory processing. Psychol. Aging 27, 410–417.
Zhang, F., Boettcher, F.A., Sun, X., 2007. Contralateral suppression of distortion product otoacoustic emissions: effect of the primary frequency in DP grams. Int. J. Audiol. 46, 187–195.
Zheng, X.Y., Henderson, D., Hu, B.H., Ding, D.L., McFadden, S.L., 1997. The influence of the cochlear efferent system on chronic acoustic trauma. Hear. Res. 107, 147–159.