Unraveling eye movement-related eardrum oscillations (EMREOs): how saccade direction and middle ear properties shape amplitude and time course

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Abstract:

Eye movement-related eardrum oscillations (EMREOs) reflect movements of the tympanic membrane that are known to scale with the magnitude and direction of saccades. While EMREOs have been consistently described in humans and non-human primates, many questions regarding this phenomenon remain open. Based on bilateral in-ear recordings in human participants we here probe a number of their properties that improve our understanding of the EMREOs' origin and functional significance. We show that the time courses are comparable between the left and right ears, and between paradigms guiding saccades by visual and auditory targets. However, the precise time course and amplitude differ significantly between ipsi- and contralateral saccades beyond the previously known phase-inversion described for saccades in opposing directions. Finally, we show that the EMREO amplitude is negatively related to the compliance of the tympanic membrane. These results altogether raise potential challenges for the interpretation of EMREOs in the light of a coordinate-alignment between vision and hearing. Furthermore, they support the notion that EMREOs largely reflect motor-related top-down signals that are relayed to the middle ear muscles in a differential principle similar as governing the execution of ipsi- and contralateral saccades.

Keywords: EMREO; saccades; sensory-motor integration; eye movement; middle ear; eardrum

1. Introduction

In-ear microphone recordings reveal rhythmic signals that are systematically aligned to saccadic eye movements and which last for about 50 to 100 ms (Gruters et al., 2018; Bröhl and Kayser, 2023; Lovich et al., 2023a). These so-called eye movement-related eardrum oscillations (EMREOs) have been described in humans and non-human primates, and reflect movements of the tympanic membrane that scale with the magnitude and direction of saccades. For instance, saccades towards locations ipsi- and contralateral to the ear in focus induce oscillations of opposing phase, which has fueled speculations whether EMREOs may reflect the spatially-specific alignment of ear- and eye-centered signals (Cho, Ravicz & Puria, 2023; Lovich et al., 2023a; Tasko et al., 2022; Caruso et al., 2021; Razavi, O'Neill and Page, 2007). Yet, many questions regarding the phenomenology, origin, and functional role of EMREOs remain unresolved (King et al, 2023; Lovich et al., 2023b).

The EMREOs must be generated by active processes in the cochlea or middle ear. One candidate is the two middle ear muscles (MEMs) i.e., the stapedius and tensor tympani muscles. These connect to the tympanic-ossicular system and adjust sound transmission in loud environments, such as during the acoustic reflex (Cho, Ravicz & Puria, 2023; Lovich et al., 2023b; Edmonson et al., 2022; Tasko et al., 2022). The stapedius and tensor tympani muscles are innervated by different cranial nerves (the seventh and the fifth, respectively) and the acoustic reflexes involve partly distinct circuits. Importantly, the pathways activating the respective motor neurons involve structures that receive multisensory and motor-related signals, whose origin remains in part unknown (Mukerji, Windsor and Lee, 2010; Borg, Counter & Rösler, 1984; Møller, 1984). Hence it is possible that sensory-motor signals related to the planning or execution of eye movements are relayed through these circuits and thereby affect the eardrum. Intriguingly, movements of the eyes towards ipsi- and contralateral directions involve opposing muscles, which are also innervated by distinct cranial nerves - the lateral rectus muscle being controlled by the sixth and the medial rectus muscle by the third cranial nerve (Pierrot-Deseilligny, 2011; Machado, 2004; Walker, Hall and Hurst, 1990). It is therefore conceivable that the middle ear muscles are governed by a similar principle, in that information about opposing saccade directions enters the pathways towards the stapedius and tensor tympani

muscles in a differential manner as well. Indeed, previous studies have noted that not only the phase of the EMREO signal but also the precise time course may differ between ipsi- and contralateral saccades (Gruters et al., 2018; Murphy et al., 2020; Lovich et al., 2023a). However, these reports are mostly descriptive and a systematic and statistical comparison of such a difference in time courses is still lacking. Furthermore, if EMREOs are functionally related to the alignment of auditory and visual spaces, these transformations should exhibit symmetry between both ears. Specifically, this would mean that EMREOs evoked by saccades in ipsilateral or contralateral directions should be comparable across ears in the same relative direction. Therefore, one goal of the present study was to establish whether ipsi- and contralateral EMREOs, and EMREOs in both ears, follow different temporal profiles, as this may provide relevant insights towards unraveling the underlying pathways and functional implications of EMREOs.

Given that the pathways towards the middle ear motor neurons may involve both descending sensory information and motor signals, it remains unclear whether external sensory signals guiding a saccade contribute to shaping the EMREO time course or whether this is only related to the motor information. Previous work has shown that EMREOs emerge in relation to visually-guided saccades, during free-viewing of images, and in darkness (Gruters et al., 2018; King et al., 2023; Lovich et al., 2023a, 2023b). If EMREOs are directly and only driven by a motor-related signal one may not expect differences between EMREOs obtained during different sensory modalities. However, task-guided and spontaneous saccades may also differ by the contributing cerebral pathways (Bon and Lucchetti, 1988; Lucchetti and Bon, 1997; Leigh and Kennard, 2004), and the presence or absence of sensory signals. This leaves it unclear whether EMREOs are purely shaped by, or reflect, the saccade-related motor information or whether they are also shaped by the presence of the sensory information about the saccade target. We addressed this question by contrasting EMREOs induced by visually and auditory guided saccades.

Lastly, if the EMREO is generated by the two middle ear muscles, it is imaginable that the strength by which the EMREO is present in an individual covaries with the mobility or functioning of the tympanic membrane. For example, reduced compliance of the tympanic

membrane to changes in air pressure may result in a reduced EMREO signal amplitude. To probe for such a relation, we combined systematic bilateral recordings of the EMREO in human volunteers with an assessment of middle ear function by tympanometry and audiometry.

Overall our results show that EMREOs are comparable between the left and right ears, are comparable when guided by visual or auditory targets, but differ clearly in amplitude and time course between saccades towards targets ipsi- and contralateral to the respective ear. Furthermore, the amplitude of the early phase of an individual EMREO is negatively related to the compliance of the tympanic membrane as obtained by tympanometry. These results help to refine an understanding of the pathways giving rise to the EMREO and raise challenges for theories proposing that EMREOs help to align visual and auditory reference frames.

2. Materials and Methods

2.1. Subjects

Overall, we collected data from 34 participants (24 females, 10 males, mean ± SD age = 27,3 ± 5,3 years) recruited among university students and community members. They participated following written informed consent and received 15 euros per hour as compensation for their time. The study was approved by the ethics committee of Bielefeld University (#2021-218). Participants were screened and selected as follows: they should not report known hearing or vision impairments (vision corrected to normal with glasses or lenses < ± 2 dpt was accepted) and no known neurological or psychiatric disorders. We visually inspected their external ear canals, performed pure tone audiometry (MADSEN Xeta, GN Otometrics) to establish air conduction hearing thresholds (at 250, 500, 1000, 2000 and 4000 Hz) and performed tympanometry (R26M, Resonance, 226 Hz probe, sweep from 200 to -300 daPa) at 500, 1000, 2000 and 4000 Hz. Ipsi- and contralateral reflexes were obtained based on the “Automatic” setting: stimuli were presented for 1 s in 5 dB steps, starting at 80 dB until the intensity that provoked a 0.05 mmho variance (indicating the trigger of a reflex), or until 100 dB (500 and 4000 Hz) and 110 dB (1000 and 2000 Hz) for ipsilateral stimulation, and 120 dB for contralateral stimulation were reached. Individuals with a pure tone audiometry (PTA) threshold average below 20 dB were considered to have normal hearing (WHO, 2020). Six participants did not complete the full experiment due to either visible ear obstructions (one participant), low performance in the task-related training blocks (two participants, see 2.3.), PTA thresholds above 20 dB (one participant) or voluntary withdrawal (two participants). For each participant, data was obtained in two sessions taking place on two different days. On each day we measured EMREOs in response to visually guided and auditory guided saccades, as explained below. As part of the experiments we also obtained data for protocols involving additional tasks, which are not reported here. After initial screening and data preprocessing (see below) we included 23 participants in the final analysis.

2.2. Experimental setup and data acquisition

The experiments were carried out in a soundproofed and electrically shielded booth with low ambient light levels. Participants were seated 100 cm away from a sound-permeable screen (Screen International Modigliani, 2 × 1 m) with their head on a chinrest. Visual

stimuli were projected (Acer Predator Z650, Acer; 60 Hz refresh rate) onto this screen. Acoustic stimuli were presented from an array of 5 free-field speakers located behind the screen (Monacor MKS-26/SW, MONACOR) positioned evenly spaced between -9 and 9 degrees azimuth. Sounds were generated from a Sound BlasterZ Soundcard (sampling rate 44100 Hz) and amplified with HeadAMP 4 (ARTcessories). Stimuli were presented using the Psychophysics toolbox (Brainard, 1997) for MATLAB (The MathWorks, 2022), which was synchronized to the recording system using TTL pulses.

In-ear microphone recordings were performed using Etymotic ER-10C (Etymotic Research) systems, as reported previously (Bröhl and Kayser, 2023). Microphone signals were pre-amplified using ER-10C DPOAE amplifiers (Etymotic Research), with gain set to +40 dB, and digitized through an ActiveTwo AD-box (BioSemi) at a sampling rate of 2048 Hz. Eye movements were recorded from the left eye using the EyeLink 1000 plus eye-tracking system (SR Research) with sampling rate at 1000 Hz. Eye-tracking calibration was performed at the beginning of the experimental session and repeated after each block using a 5-point grid. The parameters for saccade detection in the EyeLink system (“cognitive” setting) were a velocity threshold of 30°/s and an acceleration threshold of 8000°/s.

To monitor the data quality of the in-ear probes, control measurements were done before the beginning of each session. This comprised an empty-room measurement consisting of 15 seconds of silence and the presentation of 20 tone stimuli presented from the speakers (10 stimuli at 200 Hz, 10 stimuli at 200 Hz, duration 400 ms) and the same measurement repeated with the ear-probes inserted into the participants' ear canals. The baseline noise spectrum and the amplitude of the tone responses served as a parameter for adjustments to the microphone insertion and to account for differences in the effective amplification gain of each microphone. We observed a consistent difference in microphone output levels for the probes in the left and right ears in response to those test tones across participants and sessions, which we used to correct for the expected EMREO levels between ears in the subsequent analysis.

2.3. Experimental design

We obtained data for three paradigms presented in different blocks. First, we collected EMREOs in response to visually-guided saccades, similar to our previous work (Bröhl & Kayser, 2023). Here, a white dot (0.2 degree radius, on the gray background of the screen) was presented at a position of 0 degrees azimuth for a fixation period of between 900 and 1400 ms and then jumped to a random position to the left (between -9 and -3 degrees azimuth in 1 degree steps) or to the right (between 3 and 9 degrees in 1 degree steps) of the central position. Participants were instructed to fix their gaze on the dot and to follow its movement to the target position. Inter-trial intervals lasted between 1900 and 2400 ms. In each session participants performed two blocks of 140 trials each, with the directions and amplitudes of target jumps pseudo-randomized across trials. Second, we collected EMREOs in response to auditory-guided saccades. To this end, two auditory target sounds were presented (clicks of 15 ms duration, smoothed by a 12.5 ms cosine ramp; around 80 dB SPL) from the speakers behind the screen. The first sound was presented at 0 degrees azimuth, while the second was presented either to the left (at -9, -6 or -3 degrees azimuth) or to the right (at 3, 6 or 9 degrees) at a delay of 650 ms from the first. Sound locations in between two speakers were created by presenting sounds from both speakers with linearly interpolated amplitudes. A central visual fixation was presented for 150 ms with the onset of the first tone to ensure central initial fixation, but disappeared before presentation of the actual saccade target. Participants were told that the sound would only move horizontally and were instructed to make the saccade to the point on the screen matching the location of the second sound. Participants performed two blocks of 90 trials each, with the directions and amplitudes of target jumps pseudo-randomized. Lastly, participants performed four blocks comprising visually-guided saccades in conjunction with an additional sensory task, the data of which are not reported here.

2.4. Data analysis

2.4.1. Preprocessing

To extract EMREOs, the microphone recordings were epoched and aligned to the onset of each saccade as detected by the EyeLink system. The individual data epochs were cleaned based on the following criteria separately for each ear and paradigm. Epochs for which the maximal Z-score at each point in time exceeded 4.5 SDs of the overall signal

were removed. We also removed epochs in which the maximal eye position exceeded a ± 16 degree window around the central fixation dot, as the eye tracking signal was not reliable outside this range. Finally, we removed epochs for which the fixation prior to the saccade was unstable; this was defined by fixations whose horizontal eye position was outside a window of ± 3 SDs of the average fixation position across all epochs for a given participant and paradigm. At this step the data of another 5 participants had to be excluded, due to excessively noisy recordings or corrupt data files. Overall, we hence report data from 23 participants. As noted above, we corrected the relative difference in signal levels between ears to account for differences in the effective gain between left and right ear probes.

2.4.2. EMREO Analysis

The main focus was to compare the time course of the EMREOs between ears, ipsi- and contralateral saccades and between visually- and auditory-guided saccades. Given that the EMREO is best visible in the average across many repetitions of the same condition, we sought to maximize the amount of useful data for these analyses. We therefore collapsed the data from the same paradigm obtained in each session. To compare EMREOs between ears, or between ipsi- and contralateral saccades, we included all saccades in the visual paradigm, regardless of whether they were guided by the target or spontaneous. This resulted in 965.5 ± 35.4 (mean ± SEM) epochs per participant respectively. To compare visual and auditory guided EMREOs, we implemented two analyses, one focusing only on the guided saccades (those produced within 1 s of the target jump) and one including all saccades performed in each block. For the ‘guided saccades’ we obtained 212.9 ± 23.3epochs for visual and 34 ± 5.2 epochs for auditory saccades respectively. When including all saccades, we obtained 510.8 ± 39.9 epochs for the auditory guided paradigm. In this analysis we also collapsed epochs across ears for each saccade direction, as the comparison of ears had revealed no significant differences (see session 3). To relate the EMREOs to the results from the hearing screening, we defined for each participant and ear the EMREO amplitude as the sum of the total EMREO deflection (i.e. the absolute values) in a time window from 0 ms to 30 ms based on the visually guided saccade paradigm. For comparison, we repeated this analysis also based on the EMREO amplitude in a later time window (30 ms to 80 ms).

2.4.3. Statistical analysis

Group-level inference on the difference in the EMREO time course between conditions (ears, saccade directions or paradigms) was implemented using a cluster-based permutation test controlling for multiple comparisons along time (Nichols and Holmes, 2002; Maris and Oostenveld, 2007). The first level statistics was based on paired t-tests at each time point comparing the two conditions of interest within each participant. Time points with t-values reaching a first-level threshold of $p < 0.01$ were included in a clustering procedure, which were defined to require a minimal cluster-size corresponding to 7 ms. The maximum sum of each potential cluster was compared against a surrogate distribution, which was obtained by randomly flipping the sign of the condition-difference across participants for 10,000 times and recalculating the test statistics. We report significant clusters at a second-level significance of $p < 0.05$. For each cluster we report Cohen's D as a measure of effect size at the time point of maximal difference. Correlations between hearing screening and EMREO amplitude were computed across ears (hence a sample size of 23 * 2) based on the Spearman's correlation coefficient. The statistical comparison of correlation coefficients was based on a permutation test: we compared the actual difference of two correlations with the distribution of differences obtained after computing the correlations after shuffling the vectors that were correlated (based on 10000 permutations).

3. Results

We analyzed bilateral EMREO recordings obtained from 23 participants performing horizontal saccades in two paradigms, guiding these either by visual or auditory targets (Fig 1). In the following we first compare EMREOs between ears and saccade directions (ipsi- and contralateral to the recorded ear) and then compare EMREOs between visual and auditory paradigms.

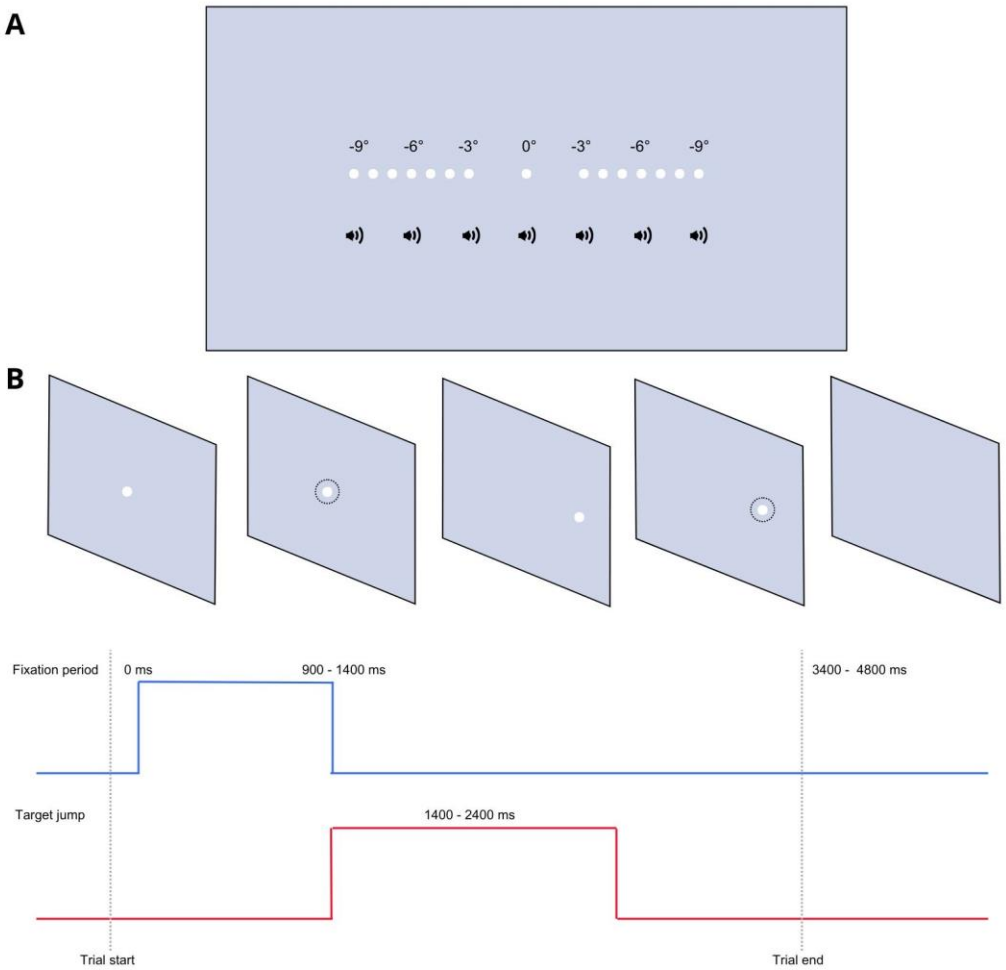

Figure 1. Schematic representation of the experiment setup. (**A**) The panel shows the target positions on the screen. The dots represent the central fixation position and the saccade targets in the visual paradigm (positions in degrees). The loudspeaker symbols represent the horizontal positions of the tones that served as saccade targets in the auditory paradigm. Panel (**B**) shows the target sequence for the visual paradigm, where the dotted circle indicates the gaze position, and the gray vertical line represents the limits of one trial. Participants were instructed to fixate their gaze on the central position as long as the dot remained on screen (for a randomly generated interval between 900 and 1400 ms, represented by the blue line). Subsequently, the central dot would disappear and either jump to one of the target positions in the visual-

guided paradigm, or sounds were presented from the respective target location in the auditory-guided paradigm. Participants then performed a saccade towards the target and had to keep the gaze fixed until the end of the trial (after the detection of saccades or 1000 ms after the start of the target jump, represented by the red line).

3.1. The EMREO time course differs between ipsi- and contralateral saccades

Previous studies have shown that the sign of the main deflections in the EMREO differs between saccades towards opposing directions (Gruters et al., 2018; Lovich et al., 2023a; King et al., 2023; Bröhl & Kayser, 2023). Our data confirm this difference in EMREO sign, but also show that the time course irrespective of this difference in sign is not the same. Figure 2A shows the group-level EMREOs for each ear and direction in the visually guided saccade paradigm, revealing initial positive (negative) deflections for ipsi- (contra) lateral saccades around 6 ms, and an opposite pattern for the second deflection around 18 to 20 ms. However, even when correcting for this difference in sign, the time courses clearly differ (Fig. 2A, solid blue line compared to the dashed orange line). This difference in time courses is shown directly in the panels below (Figure 2A, black lines).

We systematically tested for a difference in time courses across participants separately for each ear using cluster-based permutation tests. These revealed significant differences for both ears (Left: positive cluster from 16-25.5 ms, Cohen's D = 1.01, p = 0.002; negative cluster from 31.5 - 42 ms, Cohen's D = 0.60, p = 0.01; Right: negative cluster from 18-25.5 ms, Cohen's D = 0.69, p = 0.001 and 47.5 - 62.5, Cohen's D = 0.61, p = 0.0001; positive cluster from 30.5 - 42.5, Cohen's D = 1.42, p = 0.0001). Although the timing of significant differences does not allow inference about the precise time of an effect, these multiple and broad significant clusters clearly corroborate that ipsi- and contralateral EMREOs differ not only in phase but also in their overall sign-corrected time course.

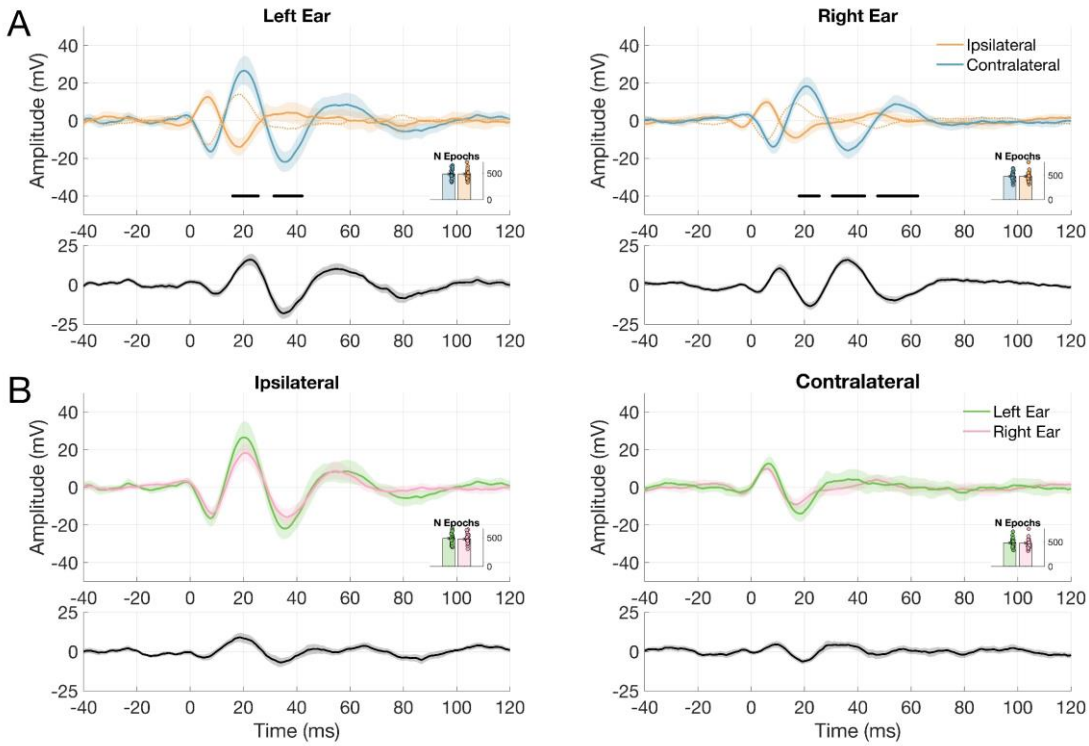

Figure 2. Group-level EMREOs ipsi- and contralateral saccades. (**A**) The upper panels show the EMREO time courses for each ear and saccade direction (solid lines); the dashed lines show the ipsilateral data after inverting the sign. The lower panels show the difference between ipsi- and contralateral directions, after sign-inverting the ipsilateral data. (**B**) Comparison of EMREOs between ears, for each of the saccade directions separately. Lines indicate the group-mean (n = 23), shaded areas the 95 bootstrap confidence interval. Black bars indicate the clusters reaching significance. Insets indicate the number of data epochs available for each participant and the group.

3.2. The EMREO time course does not differ between ears

Given that we systematically recorded EMREOs in both ears of each participant, we were able to directly compare time courses between the two. We did not expect to find differences between ears, but previous studies have also not addressed such a difference systematically using statistical analyses. Figure 2B shows the direct comparison between ears for each saccade direction separately. A statistical comparison revealed no clusters and no significant differences between ears (at $p < 0.05$; cluster-based permutation statistics) confirming that there is no evidence for a consistent difference in EMREO time courses between ears.

3.3. The EMREO time course does not differ between visually and auditory guided saccades

Then, we compared EMREOs between paradigms, guided by saccades towards visual and auditory targets. Because participants found it more difficult to perform auditory guided than visually guided saccades, we obtained fewer valid data epochs for the former paradigm. To boost statistical power for this comparison, we also collapsed EMREOs between ears (given the above results) and implemented two analyses: one including only the directly task-guided saccades, at the expense of obtaining fewer data epochs, and one including all (i.e. also spontaneous) saccades per paradigm, at the expense of statistical power by also including saccades in the auditory paradigm that were possibly also made towards visual objects in the experimental setup.

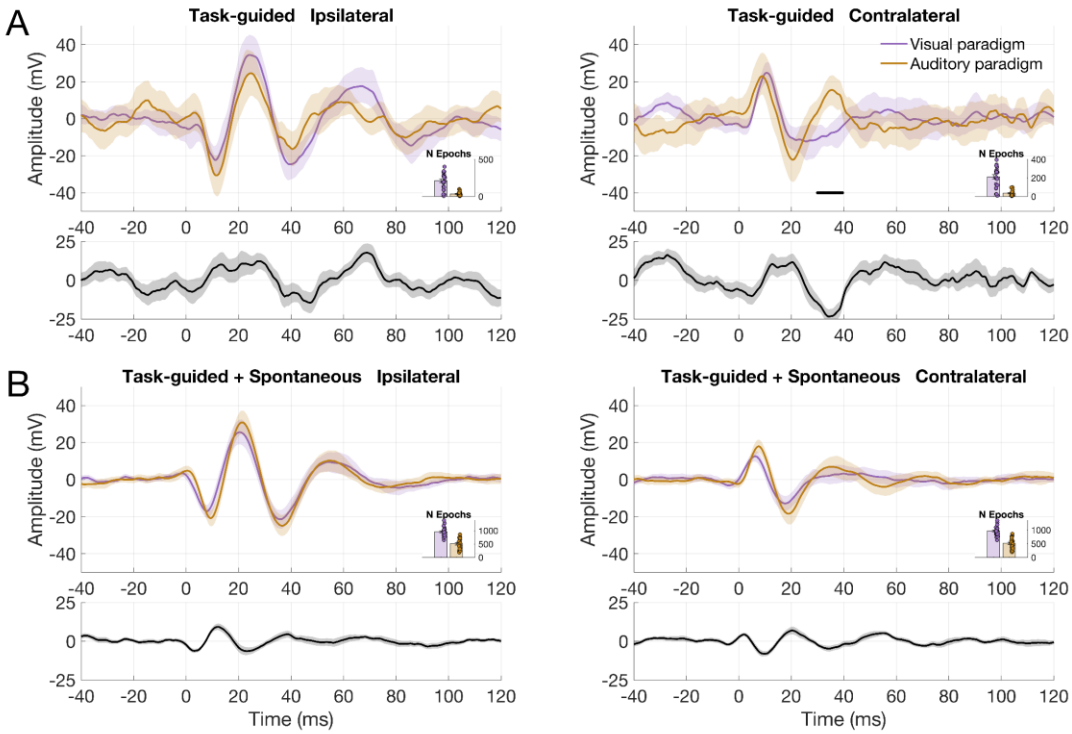

Figure 3. Group-level EMREOs for paradigms guiding saccades by visually and auditory targets. (**A**) The upper panels show the EMREO time courses for saccades towards visual (violet) and auditory (orange) targets. (**B**) Comparison between task-guided and spontaneous EMREOs in the visual and auditory target paradigm. The lower panels show the difference between ipsi- and contralateral directions, after sign-inverting the ipsilateral data. Lines indicate the group-mean (n = 23), shaded areas the 95 bootstrap confidence interval. Black bars indicate the clusters reaching significance. Insets indicate the number of data epochs available for each participant and the group.

Figure 3 shows the comparison of visual and auditory paradigms separately for each saccade direction and each of the two inclusion criteria (task-guided and task-guided + spontaneous). When considering only task-guided saccades (Fig. 3A) the EMREOs were considerably noisier and the effective number of epochs was considerably different between paradigms (see insets). A statistical comparison revealed one cluster of a significant difference between paradigms for contralateral saccades (30-39.5 ms, Cohen's $D = 0.60$, $p = 0.001$) but not ipsilateral saccades (at $p < 0.05$). When extending the analysis to include more data epochs, the EMREOs were much cleaner and the difference between paradigms was not present (at $p < 0.05$). We take this as evidence that the EMREOs are largely the same between paradigms.

3.4. Relation between EMREOs and middle ear assessment measurements

All participants had hearing thresholds consistent with normal hearing. Figure 4 shows the threshold values for pure tone audiometry and the values for the ipsi- and contralateral stapedial reflexes. Although some individuals have equivalent ear canal volume (ECV) and tympanic membrane compliance values slightly outside normal standards (Jerger, Jerger and Mauldin, 1972), the group averages are within the expected range for a normal-hearing adult population in both the right ear (ECV: mean ± std = 0.89 ± 0.49 ml; compliance: mean ± std = 0.62 ± 0.30 ml) and left ear (ECV: mean ± std = 0.80 ± 0.46 ml; compliance: mean ± std = 0.71 ± 0.42 ml). A statistical comparison revealed no significant differences between ears (Mann-Whitney test, $p = 0.55$, $U = 568.5$ for ECV; $p = 0.59$, $U = 516$ for the compliance).

Importantly, it should be noted that our sample consisted only of individuals with normal hearing, which restricts the variation in the values obtained for the PTA thresholds. While most of the participants presented reflexes within the expected values, the somewhat restrictive tympanometer settings (see 2.1.) make it possible that the true variations in reflex thresholds were more pronounced.

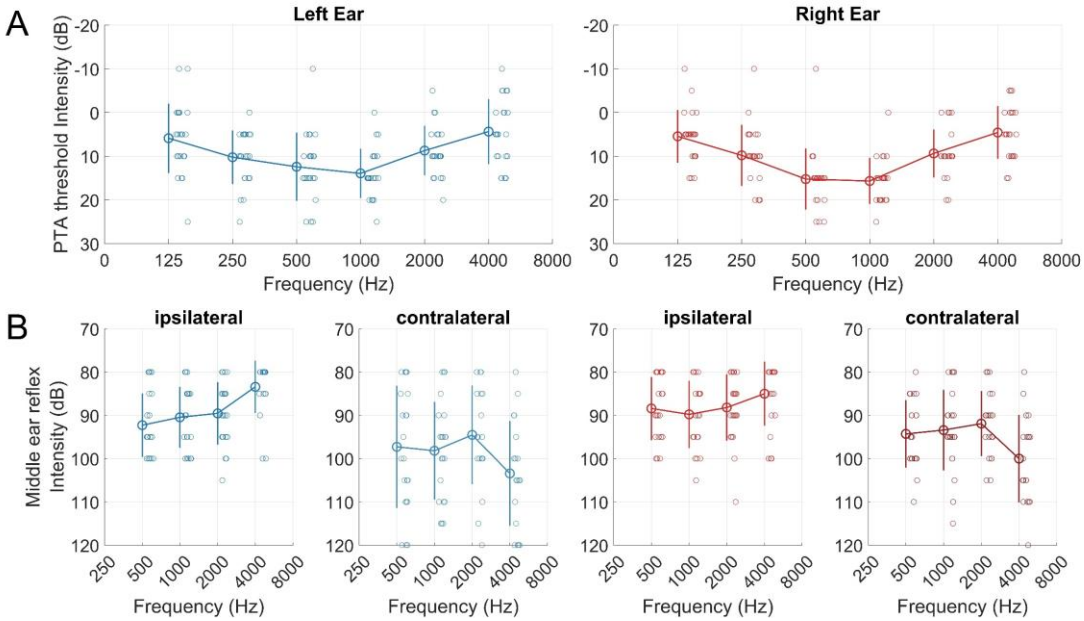

Figure 4: Pure tone audiometry and middle ear reflexes. The two panels show the subject thresholds (dots) and group means (lines) for PTA (**A**) and middle ear reflexes (**B**). In B, reflexes are divided into ipsi- and contralateral. Blue shades represent left ears and red shades represent right ears. (n = 23).

We then asked whether the EMREO amplitude was related to the functioning of the middle ear or audiological thresholds as characterized using these measurements. To test this, we extracted the overall EMREO amplitude in a window from 0 to 30 ms for each ear and participant and correlated these with these characteristics of each ear (Figure 5). This revealed a significant correlation between the EMREOs amplitude and ECV (rho = -0.38, p = 0.009, n = 46 ears) and compliance (rho = -0.44, p = 0.002, n = 46 ears), but not for PTA (rho = -0.05, p = 0.75, n = 46 ears) and reflexes (rho = 0.07, p = 0.66, n = 44 ears). Repeating this analysis for a later phase of the EMREO (30-80 ms) did not revealed any significant correlation (ECV: rho = -0.06, p = 0.67; compliance: rho = -0.17, p = 0.27; PTA: rho = - 0.17, p = 0.26; and reflexes: rho = -0.11, p =0.47). Given that the early EMREO amplitude does correlate significantly with middle ear compliance and the later phase does not, we also directly tested whether these two correlations indeed differ significantly from each other: a permutation test revealed that these differ indeed significantly (p = 0.01). Hence, the early but not the late phase of the EMREO correlates with middle ear compliance.

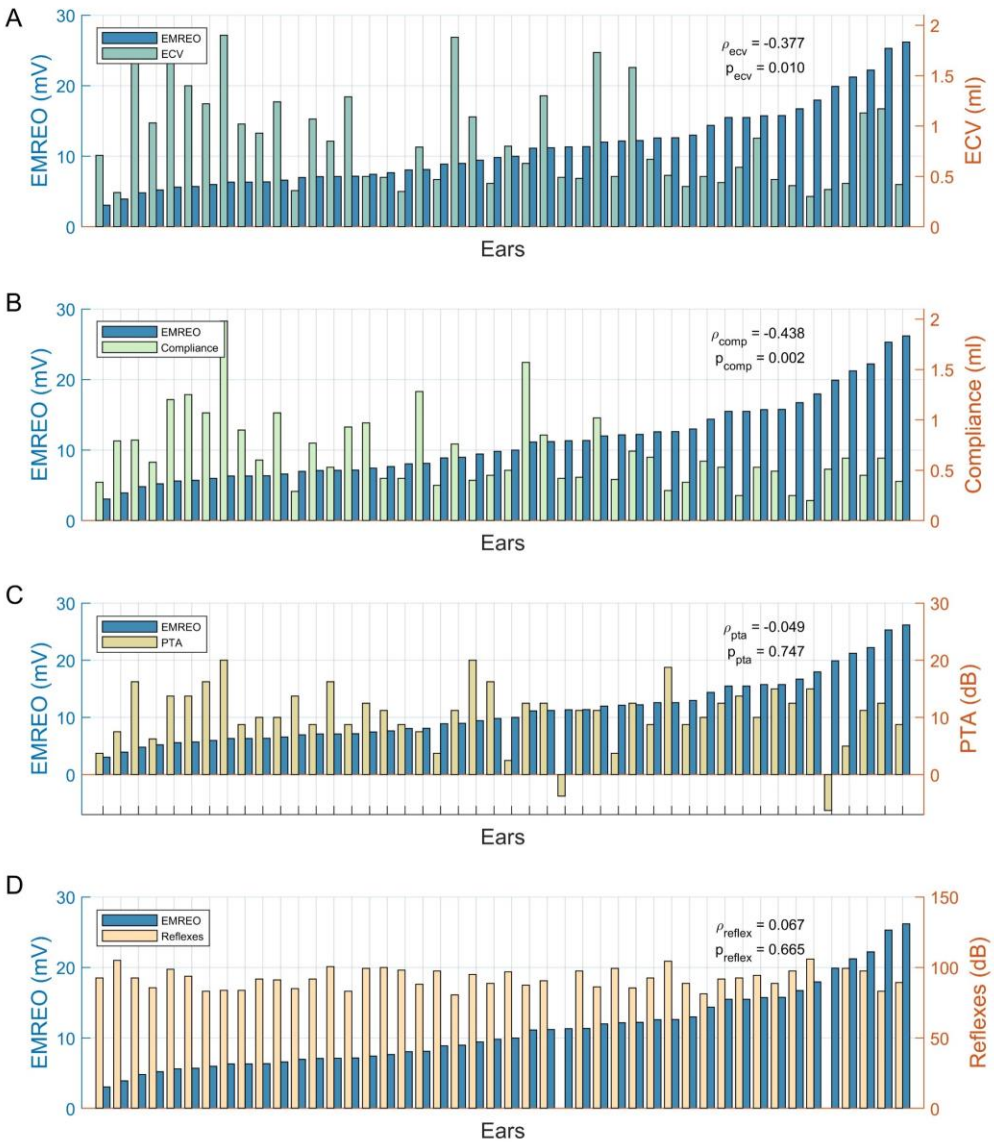

Figure 5. EMREO amplitude compared to PTA, tympanometry and reflexes. The panels show the overall EMREOs amplitudes (in the time window of 0 to 30 ms) against the measured variables. All data points were rearranged in ascending order for the EMREO amplitudes in individual ears (n = 46 in A, B and C, n= 44 in D as for one subject it was not possible to record acoustic reflexes). Pairs of bars represent data for the same ear. In all panels the left y-axis displays the scale for the EMREO amplitudes (in mV), while the right y-axis in (**A**) displays the scale for equivalent ECV (in ml), in (**B**) displays the tympanic compliance (in ml), in (**C**) displays the PTA mean thresholds for 500, 1000, 2000 and 4000 Hz (in dB) and in (**D**) displays the mean reflex thresholds for ipsi- and contralateral at each frequency (in dB). Spearman's correlation rho and p-value are shown in each panel.

4. Discussion

Eye movement-related eardrum oscillations have been described in a number of recent studies, though their origin and precise function remain unclear. The overall time course of the EMREOs observed here is qualitatively similar to that reported in previous work (Gruters et al., 2018; Lovich et al., 2023a; King et al., 2023; Bröhl & Kayser, 2023). Characteristic features are prominent deflections of latencies just prior to 10 ms and around 20 ms following saccade onset, with an opposing phase in the left and right ears for saccades in the same direction. While previous studies noted that EMREOs look overall similar between left and right ears, most studies recorded only a single ear per participant, which precludes a direct statistical comparison. Based on the systematic recording of EMREOs in both ears, we here show that indeed the time course and amplitude is comparable between ears.

4.1. EMREO time course differentiates ipsi- and contralateral saccades

The opposing phase of the EMREO between ears for a given saccade, and the opposing phase for ipsi- and contralateral saccades within each ear, have led to the notion that the EMREO reflects a spatially specific process potentially reflecting processes serving the spatial alignment of eye and ear-centered visual and auditory signals. Indeed, the EMREOs scale both with saccade direction and saccade size, and do so both in horizontal and vertical directions (Murphy et al., 2020; Lovich et al., 2023a). If for a given time point the amplitude of the EMREO deflection would be determined by the saccade amplitude and its sign by the direction, reading out such a spatially specific transformation would be straightforward. However, previous studies have noted that the precise EMREO time course may differ between saccades to ipsi- and contralateral targets (Lovich et al., 2023a, King et al., 2023, Bröhl & Kayser, 2023). The present data corroborate this and demonstrate a clear and statistically significant difference, which is most pronounced for the later portion of the EMREO, starting at around 30 ms. Here, our data reveal a larger deflection for contralateral saccades compared to the distinctively smaller deflection for ipsilateral saccades. This difference in EMREOs for opposing saccade directions could be meaningful for two reasons.

First, it may provide insights about the pathways generating the EMREO. Saccades are conjugated eye movements that involve the simultaneous contraction of agonistic and relaxation of antagonistic muscles to facilitate coordinated motion. During ipsilateral saccades, synchronized contraction is mediated by the abducens nucleus, while the contralateral paramedian pontine reticular formation inhibits opposing muscles, demonstrating the distinct neural complexes engaged in relaying differential activation patterns to extraocular muscles (Purves et al., 2001). Similarly, the two middle ear muscles are innervated by different cranial nerves as well (the fifth for the tensor tympani and the seventh for the stapedius), but there seems to be less knowledge about potential projections from the centers controlling ocular muscles to the pathways controlling the middle ear muscles. Though previous studies have noted that stapedius motor neurons are responsive to non-acoustic sensory signals (Tasko et al., 2022; Deiters et al., 2019; Salomon and Starr, 1963), the pathways and nature of potential non-acoustic inputs to the middle ear motor neurons remain unclear. Given the opposing activation patterns that control saccadic eye movements, one may speculate whether the spatial opposition is similarly transferred onto the pathways that innervate middle ear muscles, hence giving rise to distinct EMREO time courses.

Second, this result poses a challenge for the hypothesis that the EMREO aids in coordinating transformations between visual and auditory reference frames. While the data do not rule out that the EMREO contributes to such a transformation per se, they suggest that such a link may not be based on a straightforward linear relation. This holds true in particular for the later phase of the EMREO i.e., beyond 30 ms, where our data show clear differences in time course between saccade directions. Like many questions regarding the EMREOs, it also remains unclear how meaningful this late portion of the signal is. For example, it could be that the damped oscillatory signal that one obtains with in-ear microphone recordings directly corresponds to an oscillatory drive exerted on the tympanic membrane. Alternatively, it could be that the tympanic membrane simply rings in response to an abrupt stiffening or relaxation induced by changes in the tension of a particular muscle, as was theorized by Cho and colleagues (2023) while investigating isolated stapedius or tensor tympani contraction effects on the eardrums. While a difference in time courses suggests a difference in the driving cause, this makes it difficult

to interpret the precise change in state of the tympanic membrane in response to saccades. Therefore, more focus is required to investigate the generative processes that give rise to the EMREOs as they are observed using in-ear recordings, to better understand whether indeed EMREOs fulfill some kind of coordinate alignment between vision and hearing.

4.2. EMREOs scale with eardrum compliance and ear canal volume

We found that the EMREO amplitude in the early phase correlates negatively with the ear canal volume and the compliance of the tympanic membrane. The relation to ear canal volume may simply reflect an acoustic phenomenon whereby a larger canal has a larger acoustic impedance, while the relation to the compliance might be more meaningful. It is possible that some tympanic membranes are under stronger tension from the MEMs and thereby show a lower compliance. If the EMREO is generated by the MEMs, stronger tension could indicate greater control of the membrane by those pathways. Hence, while some ears may exhibit a stronger influence from the pathways driving EMREOs and thus reduced flexibility others may show the opposite. Alternatively, the differences in compliance might be due to a more rigid ossicular chain. This could passively lead to larger amplitudes if the tympanic membrane is more sensitive to ringing at eigenfrequencies closely related to that of EMREOs, or in larger amplitudes if the underlying process includes an active overcompensation to counteract an otherwise less variable sound transduction. Still, it is not immediately clear how this would lead to a differential correlation of early and late EMREO amplitudes with compliance. As noted above, one possibility is that the earlier phase is more directly related to the actual phenomenon and the later phase reflects simply the ringing of the membrane in response to an abrupt stiffening or relaxation. If this was the case the earlier phase of the EMREO would be possibly more meaningful when studying its function.

4.3. EMREOs relate to motor but not sensory signals

Our data also show that the EMREO is comparable when a saccade is made towards a visual target to when saccades are guided by a sound. This independence of EMREOs from the precise experimental paradigm fits with previous work reporting EMREOs obtained during spontaneous viewing of images or in darkness (Lovich et al., 2023b).

Overall, this suggests that the EMREO is mostly related to the motor act of a saccade and not exogenous sensory information. This conclusion is also supported by our previous study where we showed that the presence of an attentional cue did not systematically alter the EMREO (Bröhl and Kayser, 2023).

The motor link between eye movements and the EMREOs relates to a larger topic of extrinsic auricular muscle synkinesis in relation to gaze movements (Wilson, 1908; Carmichael and Critchley, 1924, 1925; Schmidt & Thoden, 1978). Developmentally, the cranial nerves controlling eye movements, the middle ear muscles and those controlling the auricular muscles all share the same premandibular mesoblastic origin (Carmichael and Critchley, 1925). The circuits activating the auricular muscles overlap with those most likely giving rise to the EMREO. The postauricular reflex, wherein the posterior auricular muscle activates in response to loud sounds, is supposedly guided by acoustic signals related to the facial motor nucleus from the ascending auditory pathways via the lateral lemniscus, but also indirectly via the reticular nucleus from the superior colliculus (Liugan, Zhang and Cakmak, 2018; O'Beirne and Patuzzi., 1999; Yoshie and Okudaira, 1969). The latter opens the pathway for signals relating to eye movements but also visual stimuli to activate auricular and possibly also middle ear muscles. While future work needs to define the precise contributions of the two middle ear muscles to the EMREO and the pathways controlling the EMREO, the broader topic of how non-acoustic information shapes the muscles in and around the ear remains exciting.

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