Conserved features of eye movement related eardrum oscillations (EMREOs) across humans and monkeys

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Abstract:

Auditory and visual information involve different coordinate systems, with auditory spatial cues anchored to the head and visual spatial cues anchored to the eyes. Information about eye movements is therefore critical for reconciling visual and auditory spatial signals. The recent discovery of eye movement-related eardrum oscillations (EMREOs) suggests that this process could begin as early as the auditory periphery. How this reconciliation might happen remains poorly understood. Because humans and monkeys both have mobile eyes and therefore both must perform this shift of reference frames, comparison of the EMREO across species can provide insights to shared and therefore important parameters of the signal. Here we show that rhesus monkeys, like humans, have a consistent, significant EMREO signal that carries parametric information about eye displacement as well as onset times of eye movements. The dependence of the EMREO on the horizontal displacement of the eye is its most consistent feature, and is shared across behavioral tasks, subjects, and species. Differences chiefly involve the waveform frequency, and may relate at least in part to differences in the speed of eye movements across species.

Introduction

Linking visual and auditory space requires information about eye movements. Spatial cues to sound location involve interaural level differences (ILDs) and interaural timing differences (ITDs), cues that can be used to determine the positions of sounds with respect to the head, or a head-centered reference frame. In contrast, the locations of visual stimuli are detected via the pattern of light on the retina, an eye-centered reference frame. In short, every time the eyes move, the retina shifts with respect to the head and ears, changing the relationship between eye-centered visual spatial cues and head-centered auditory spatial cues. Thus, the brain must keep track of eye movements to resolve the difference between these two coordinate systems and support binding of visual and auditory stimuli based on their location (e.g.(Groh and Sparks, 1992; Groh, 2014)).

Early work on how the brain achieves reference frame alignment was conducted via single unit recordings in rhesus monkeys. In the superior colliculus, changes in eye position were found to cause auditory receptive fields to shift their positions with respect to the head (Jay and Sparks, 1984, 1987a; Lee and Groh, 2012); (see also see also see also see also Hartline et al., 1995; Zella et al., 2001; Populin et al., 2004). This suggested that a coordinate transformation of auditory signals was occurring somewhere within the brain (Groh and Sparks, 1992). Subsequent work extended these observations to other multisensory brain regions such as the frontal eye fields (Russo and Bruce, 1994; Caruso et al., 2019) and parietal cortex (Stricanne et al., 1996; Cohen and Andersen, 2000; Mullette-Gillman et al., 2005, 2009). Intriguingly, effects of eye position were also found in predominantly auditory brain regions such as auditory cortex during responses to sound stimuli (Werner-Reiss et al., 2003; Fu et al., 2004; Maier and Groh, 2010) and the inferior colliculus (Groh et al., 2001; Zwiers et al., 2004; Porter et al., 2006; Bulkin and Groh, 2012b, a; Willett et al., 2019).

These reports concerning eye movement effects on auditory responses in auditory brain regions motivated our foray into the most peripheral part of the auditory system, the ear itself. We reasoned that information about eye movements could be conveyed via the descending pathways to the motor actuators within the ear, such as the middle ear muscles and the outer hair cells, and

that, just like with conventional otoacoustic emissions and middle ear reflex testing (e.g. (Kemp, 1978; Shera, 2004; Schairer et al., 2013)), the impact of such signals might produce movements of the eardrum that could be detected by microphones in the ear canal. This led to the discovery of eye movement-related eardrum oscillations (EMREOs) (Gruters et al., 2018; Murphy et al., 2020; Lovich et al., 2022; King et al., submitted).

EMREOs occur with saccades, time-locked and slightly preceding their onset, and show phase-setting at offset, extending for at least several tens of milliseconds after the eyes stop moving. The waveforms of EMREOs carry precise and parametric information about the direction and amplitude of the saccade (Lovich et al., 2022). EMREOs occur in the absence of incoming sound, and how they (or more properly, the underlying mechanism they reflect) impact sound transduction is unknown. It is also unknown how they might contribute to the eye movement-related modulation of sound responses observed later in the brain's auditory pathway.

Intriguingly, EMREOs are seen in both humans and rhesus monkeys (Gruters et al., 2018). A quantitative comparison between the human and monkey EMREOs can therefore serve as a natural experiment to shed light on which features of the EMREO are most likely to be functionally important to auditory coordinate transformations or any other potential purpose. This human-monkey comparison is particularly apt because the two species have similar visual and auditory acuity and similar eye movements (e.g., Jay and Sparks, 1990). They are also known to integrate visual and auditory space in reasonably similar ways, showing similar thresholds for fusing vs. distinguishing visual and auditory locations (Mohl et al., 2019). Features of the EMREO that are shared across humans and monkeys may represent aspects that are particularly important for these shared perceptual and oculomotor attributes. In short, a quantitative cross-species comparative analysis can shed light on the function and underlying mechanism of this phenomenon, and is a needed advance over the qualitative assessment provided in our initial study (Gruters et al., 2018).

We report here that EMREOs in both humans and monkeys exhibit a similar dependence on the horizontal displacement of the eye during the accompanying saccade. Differences across species include the frequency of the EMREO signal, which could be related to differences in the velocity

of eye movements between humans and monkeys, consistent with what would be expected of a signal arising from a corollary discharge of an eye movement command. Further, EMREOs were similar across different task designs, suggesting that they are associated with the eye movements regardless of how the eye movements are elicited. We hypothesize that the horizontal eye displacement signal reflected in EMREOs may be used during auditory localization and perception, specifically to tailor interaural timing and level difference cues to sound location in an eye movement dependent fashion.

Methods

Participants

We recorded eye movement-related eardrum oscillations (EMREOs) simultaneously in the left and right ears of 4 monkeys (3 female, 1 male) and 4 human subjects (2 female, 2 male). All procedures involving human subjects were approved by the Duke University Institutional Review Board. All procedures involving monkey subjects were performed in accordance with an animal protocol approved by Duke University IACUC. Subjects had apparently normal hearing and normal or corrected vision. Informed consent was obtained from all human participants before testing, and all human participants received monetary compensation for participation.

Tasks

Monkey behavioral task: To maximize the rate of data collection in the monkeys and permit the testing of relatively untrained animals, we allowed monkeys to freely view a black monitor screen and make saccades wherever and whenever they wished (free-viewing saccade task). The black screen made capturing the pupil of the monkey easier and more accurate because of size of the pupil in darkness. The free viewing task allowed us to test any of the available monkeys in our colony regardless of their training status. No external sounds were presented.

Human behavioral tasks: Since our previous study involved performance of visually guided saccades to specific targets (Gruters, Murphy et al. 2018), but the monkey testing for the present study involved free viewing, we tested our human subjects on both a visually-guided saccade task similar to the one we used before (Figure 1a) and a free-viewing task (Figure 1b) similar to the one used for monkeys (Figure 1c). Humans viewed abstract Jackson Pollock paintings, which helped them stay awake and engaged throughout the task. They made saccades wherever and whenever they wished, similar to the monkeys. This permitted us to establish whether different tasks affect the EMREO signals (in humans) and to compare the monkey and human results using a free-viewing task. No external sounds were presented during either task.

Sessions, Head Restraint, Eye Tracking, and Saccade identification:

Sessions: A microphone (Etymotic ER-10B+) was placed in each ear of the subject while they made saccades (figure 1d). In a given session, human subjects performed 3 blocks (5 minutes/ block) of the visually-guided saccade task interleaved with similar length blocks of free viewing, for a total of six blocks. Each session lasted approximately one hour. Microphones (48 kHz sampling rate) were assessed prior to each session by placing each microphone into a test tube and playing a frequency sweep from 10Hz to 2kHz through the associated earbud speaker (pure tone sweep from 10-1600Hz: 10Hz steps for 10-200Hz, 100Hz steps for 300-1000Hz, 200Hz steps for 1200-2000Hz). Microphones were also assessed before every block of a session using the same frequency sweep while in the ears of the subject. Monkey sessions lasted about 60-180 minutes. Human participants were tested in a total of 3-5 sessions each and monkeys were tested in 20-30 sessions.

Head restraint and eye tracking: Head movements were minimized in human participants with a chin rest and in monkey participants using a surgically implanted head post. Surgical implantation was accomplished under general anesthesia, aseptic conditions, and with suitable analgesics to minimize discomfort in accordance with IACUC regulations. Eye movements were monitored in both humans and monkeys using the same eye tracking system (EyeLink1000), with eye position sampled at 1000 Hz. In human subjects, the eye tracking system was calibrated based on saccades to visual targets. In the monkeys, this calibration was not performed but

similar settings (brightness, pupil size, cornea size) to those of the human sessions were used. As described further below, the data analysis methods used were robust to differences in these calibration procedures.

Initial analysis steps for microphone and eye tracking data

After collection, microphone data were downsampled from 48 kHz to 2 kHz for further analysis. These data were otherwise unfiltered. Saccade onsets and offsets were identified based on the rate of change in eye acceleration (third derivative, or "jerk"). After smoothing with a 7 point filter (7 ms), the first peak of the jerk was considered to be saccade onset and the second peak of the jerk was considered to be saccade offset (Murphy et al., 2020) (Lovich et al., 2022).

Data inclusion criteria and normalization of signals across subjects/sessions:

Data could be excluded at the session/block level or at the trial/saccade level. At the session/block level, data for the entire session/block were excluded if the assessment of the microphone via frequency sweep for that session or block indicated any major issues, such as a possible shift in the position of the earbud assembly. Within each session and block, individual trials or saccades could be excluded on the basis of the eye tracking data. Trials/saccades were excluded if there was less than 200 ms of steady fixation before saccade onset or after saccade offset. Saccades could also be excluded if the saccade curvature was too great (more than 4.5º of subtended angle). After these screens were applied, we also excluded individual trials based on whether the RMS noise level on individual trials exceeded a criterion value (0.02, arbitrary units, set based on inspection of the normal RMS range in quiet recording sessions). We also excluded trials if the maximum or minimum microphone value on that trial was more than 10 standard deviations from the mean microphone value in that session or block. Overall, these exclusion criteria served to minimize the inclusion of trials in which the monkey generated noise via fidgeting or other behaviors. The same criteria were applied to both human and monkey sessions. After these exclusion criteria were applied, we then computed the Z-scores of the microphone values relative to a pre-saccadic baseline (-100 to -40 ms prior to saccade onset). Results in the present study are therefore expressed in units of standard deviation relative to this baseline period.

Figure 1

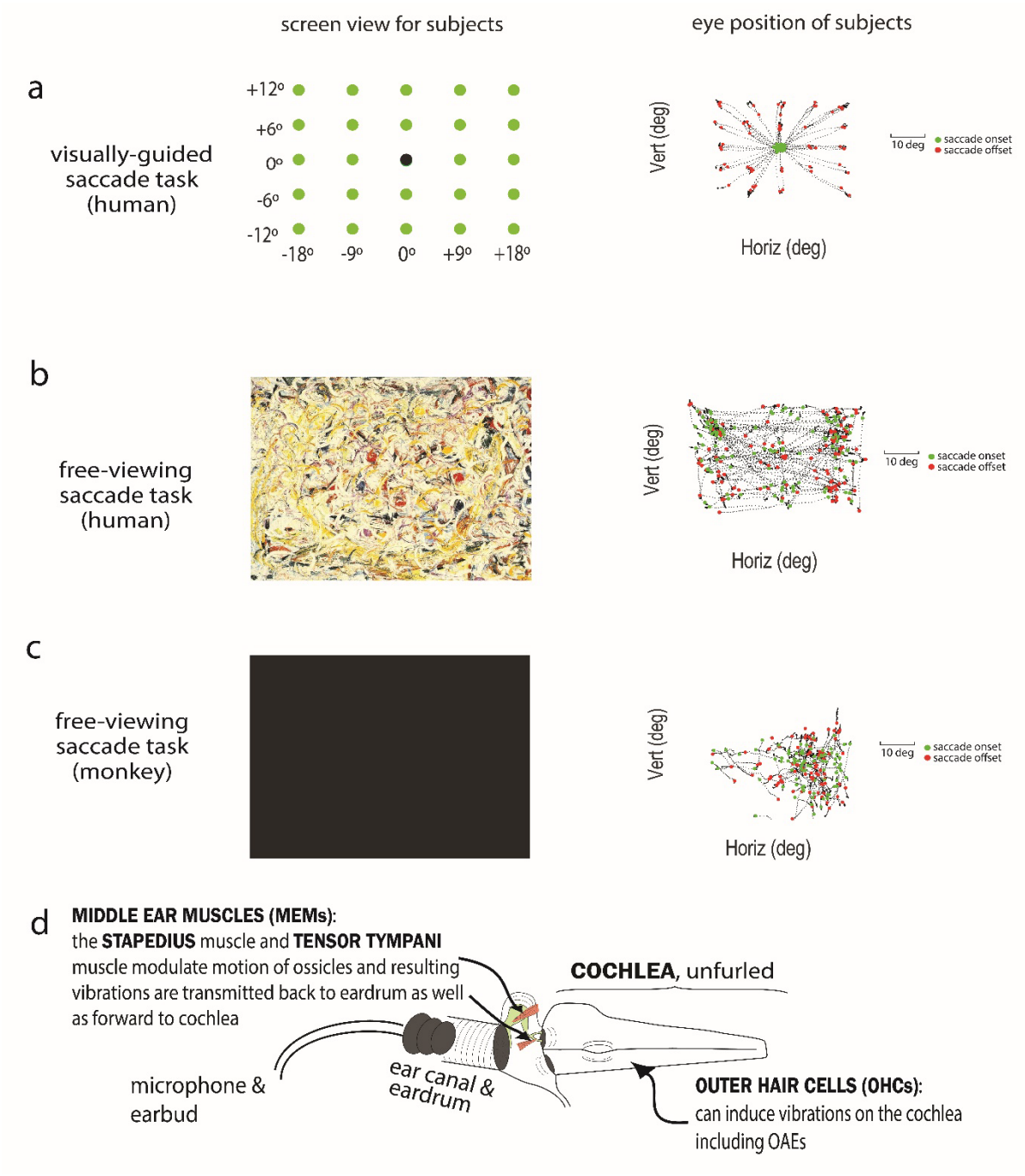

Figure 1: Task and microphone setup.
1a. Humans performed a visually-guided saccade task in which the black fixation dot appeared on the screen for 750 ms. The black dot would then disappear and one of the green dots would appear for 750 ms. Subjects had to saccade to the green dot and fixate for a minimum of 200 ms at which point the dot would turn red signaling that the trial was over. An example of one subject's eye position during one block can be seen on the right. 1b. Humans performed a free-viewing saccade task interleaved with the visually-guided saccade task in which they made saccades in any direction and magnitude of their own volition. An example of one subject's eye position during one block can be seen on the right. 1c. Monkeys performed the same free-viewing task as humans but with a black screen. An example of one monkey's eye position during one block can be seen on the right. 1d. A microphone was

placed into each ear canal of the subject and recorded pressure changes of the eardrum while the subject made saccades. No external sounds were presented.

Data Analysis

Extending/replicating our previous methods (Gruters et al., 2018; Lovich et al., 2022), we fit the raw EMREO signal collected in each ear to a linear regression model that includes the basic parameters of each eye movement:

$$Mic(t) = B_{\Delta H}(t)\ \Delta H + B_{\Delta V}(t)\ \Delta V + B_H(t)\ H + B_V(t)\ V + C(t)$$

The first four terms concern the change in eye position relative to the starting position for each saccade in the horizontal and vertical dimensions, and are measured in degrees. Specifically, these terms concern the horizontal displacement of the eye (ΔH), vertical displacement of the eye (ΔV), the horizontal initial position (H), vertical initial position of the eye (V). Time-varying coefficients $B_{\Delta H}(t)$, $B_{\Delta V}(t)$, $B_H(t)$, and $B_V(t)$ were fit to these parameters. The final term is a time-varying constant component (C(t)) that captures everything else left in the signal. C(t) can be thought of as the best fitting average oscillation across all eye positions and displacements.

This regression model allows us to analyze the EMREO with respect to the individual parameters of the synchronous eye movement and is largely robust to the particular task involved, except that the initial position parameters will mainly capture fixational scatter in the visually-guided saccade task versus a much larger range of initial positions in the free viewing tasks. Thus, we do not necessarily expect perfect correspondence of the initial position terms of the regression fits across these two tasks; any small differences in the accuracy of eye tracking calibration will also affect the precise values of these coefficients. From related work (Lovich et al., 2022; King et al., submitted), we know that the EMREO waveform depends most strongly and consistently on the horizontal displacement of the eyes, and that this dependence superimposes on a considerable constant component in human participants. Therefore, we will focus on the regression coefficient for horizontal displacement and the constant component when comparing humans and monkeys.

Results

In the human participants, we first confirmed that task performance had little impact on key aspects of the EMREO signal. We found that the regression coefficients of horizontal displacement (*ΔH)* and the constant component (C) across four human subjects while they performed the visually-guided saccade task (purple) and the free-viewing saccade task (green) were similar (Figure 2a, data from 4 right ears). While different subjects showed different oscillatory patterns, the overall pattern was generally very consistent within subjects across tasks. The thick parts of the EMREO signal in Figure 2a-b indicate the time periods when the regression coefficient differed significantly from zero with 95% confidence, and the shaded areas are the SEM of the EMREO. The horizontal displacement regression coefficient (Figure 2a) generally differed from zero for several tens of milliseconds starting at saccade onset except where it crossed zero as it transitioned between a peak or a trough, but there was little notable difference across tasks. The constant term showed more variation across subjects (Figure 2a bottom row) but was still quite similar within each subject for each task. Overall, these results indicate that an oscillatory dependence on horizontal saccade amplitude occurs across all subjects and for both visually-guided and free-viewing saccades, with some variation in the timing, amplitude, precise waveform, and presence/magnitude of the constant component. This pattern is consistent with our previous work (Gruters et al., 2018; Murphy et al., 2020; Lovich et al., 2022; King et al., submitted), and suggests that the free-viewing saccade task is an equally effective way to collect EMREO data.

Figure 2b shows corresponding findings for the right ears of four monkey subjects while they performed the free-viewing saccade task (black). Like the human data, the EMREO is strongly dependent on the horizontal displacement of the associated eye movement (Figure 2b top row). The oscillation co-varies in phase and amplitude similarly to the signal recorded in humans. Like the humans, the waveform varied to some extent across subjects, but all showed a sharp onset at (or slightly before) saccade onset, continuing for at least one full oscillatory cycle, and all subjects had a significant signal at some points in the first few tens of milliseconds after saccade onset. Similar to the human data, the constant component varied across monkey subjects more than the horizontal component. While some subjects have clear, significant oscillations in the constant component (Monkey F and Monkey U), others have a much noisier signal (Monkey Y) (Figure 2b bottom row). The constant component of the monkeys also differs from the

humans in that the largest positive peaks occur later in the time course of the EMREO (around 75 ms-100 ms) compared to within the first 50 ms after saccade onset in humans.

Figure 2

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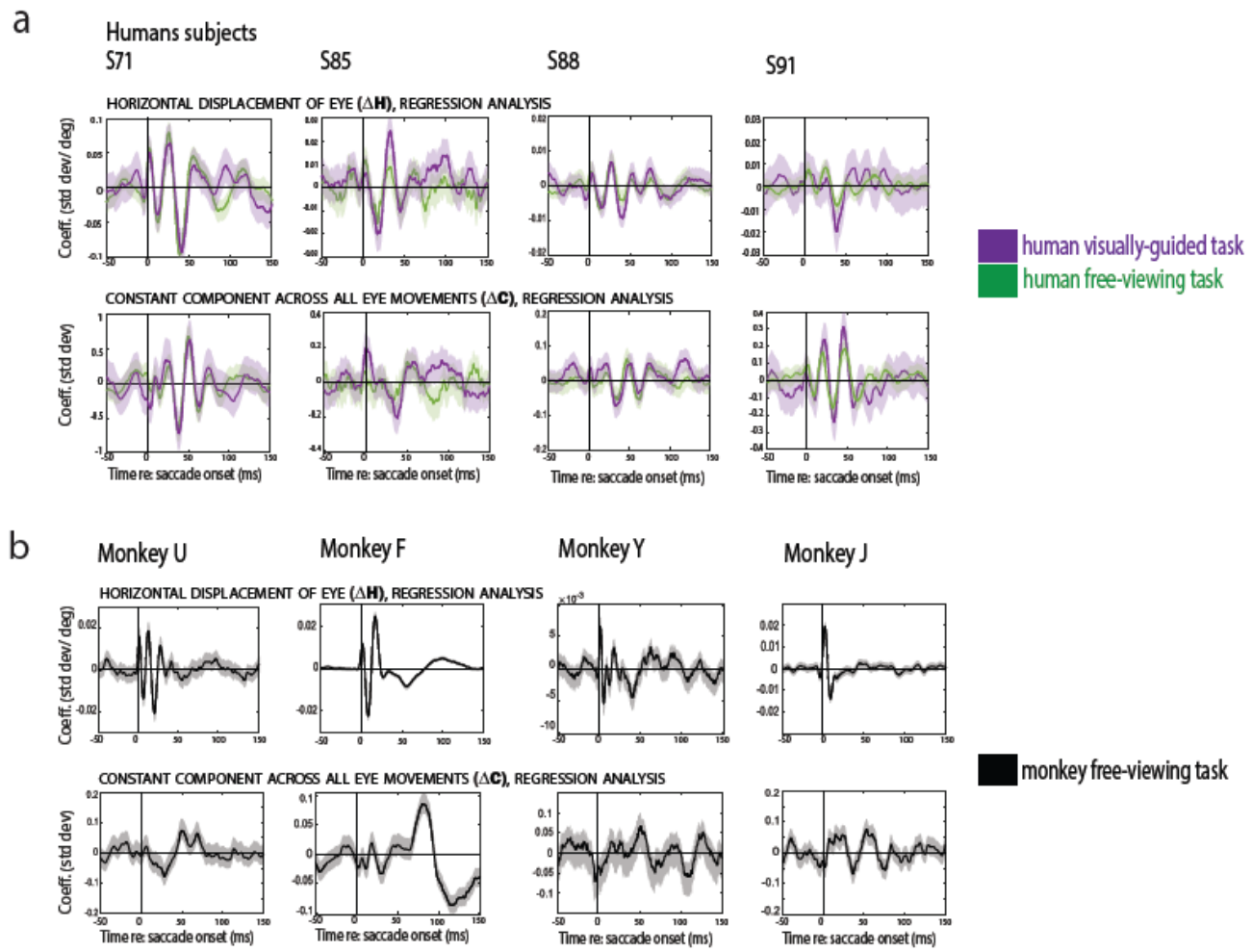

Figure 2: Regression analysis and individual subject data.
2a. The regression coefficient reflecting the influence of horizontal displacement of the eye on the EMREO signal (top) and the constant component (bottom) in the right ears of humans across both tasks (visually-guided in purple and free viewing in green). 2b. Similar to (a) but for the right ears of monkeys during the free-viewing task.

The chief difference between the horizontal displacement regression coefficients in human vs. monkeys was in the time course. In Figure 3a, we plot the average of all human data for both

the visually-guided saccade task (purple) and the free-viewing saccade task (green) as well as the monkey data for the free-viewing saccade task (black), aligned to onset of the saccade. The oscillation initially occurs at a higher frequency for the monkey responses than the humans, and this rapid oscillatory portion then transitions to a several much slower peaks/troughs.

The chief difference for the constant component in humans vs. monkeys was its magnitude (Figure 3b). While the human data has clear significant peaks and aligns in phase at the onset of the saccade for both tasks (purple: visually guided; green: free viewing), there is no comparably consistent signal in the monkey data. As seen in Figure 2, some individual monkeys (Monkey F and Monkey U) have significant positive and negative peaks between 50-100 ms, very different from what we see in the humans. The other two monkeys have no peaks in the constant component that are significantly different from zero, and therefore the average across the monkeys is much smaller than for the humans. It is unclear why this could be different across monkeys or why the monkeys as a group should differ from the humans in this regard.

The faster time course of the monkey EMREO compared to humans may relate to the faster time course of monkey saccades. As shown in Figure 3a-b, the saccades of the monkeys were shorter in duration than those of the humans (black vs purple vs green bars at the top of the graphs). It is known that monkeys make faster saccades than humans (compare findings in: (Bahill et al., 1975; Jay and Sparks, 1990; Groh and Sparks, 1996; Guadron et al., 2022)), and this was true in our participants as well. Figure 3c shows the peak speed of saccades as a function of their amplitude, averaged across monkeys (black) and across humans performing the free viewing task (green). On average, monkeys had faster saccades than humans at all corresponding amplitudes. There was little difference among the humans as a function of the task (Figure 3d).

These findings indicate that the dependence of the EMREO on the horizontal displacement of the eye movement is quite conserved across humans and monkeys, differing mainly in the time course of the oscillation that may be related to difference in saccade peak speed.

Figure 3

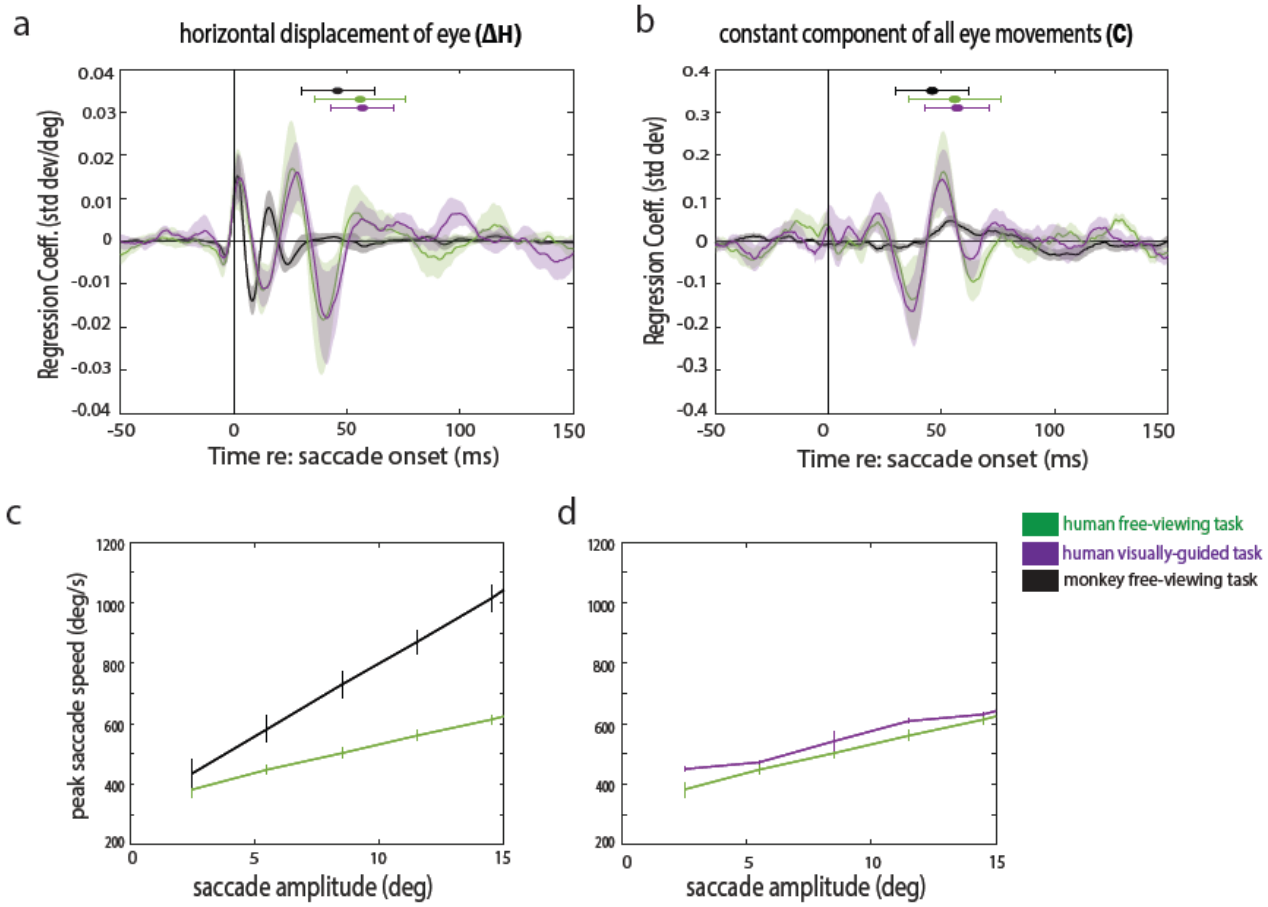

Figure 3: Average EMREO signal and relationship to saccade duration/speed. (a-b). Average EMREO regression coefficients across both left and right ears of human visually-guided saccades (purple), human free-viewing saccades (green), and monkey free-viewing saccades (black). The regression coefficient concerning horizontal displacement of the eye is plotted in (a) and the constant component is plotted in (b). Regression coefficients were first averaged within each subject ear and then averaged together across all humans or all monkeys; the horizontal dimension was flipped for the left ear in order to combine all left and right ear data. 3c-d. Moving averages of the monkey saccade velocities (black) and human free-viewing

saccade velocities (green) with respect to saccade amplitude(c) and moving averages for saccade velocities with respect to saccade amplitudes for humans during both tasks(d).

Discussion

Sounds and visual stimuli are detected in different "native" coordinate systems. The location of a sound is computed from cues involving loudness and timing differences across ears (interaural loudness differences or ILDs; interaural timing differences or ITDs), as well as variation in spectral frequency as a function of location with respect to the ears. These cues yield location information in a head-centered reference frame. The location of a visual stimulus is ascertained from the pattern of light hitting the retina, producing cues in an eye-centered reference frame. Information about the position and movements of the eyes with respect to the head is therefore necessary before the locations of visual and auditory stimuli can be matched up with one another. Understanding how the brain incorporates this information to reconcile these different coordinate systems is critical to knowing how the brain links information across the visual and auditory systems.

Research into the intersection between eye movements and hearing has involved psychophysical studies in humans (e.g. (Weerts and Thurlow, 1971; Lewald and Ehrenstein, 1996; Lewald, 1997, 1998; Boucher et al., 2001; Lewald and Ehrenstein, 2001; Lewald and Getzmann, 2006; Pavani et al., 2008; Klingenhoefer and Bremmer, 2009; Collins et al., 2010; Krüger et al., 2016; Willett et al., 2019)) and neurophysiological studies in monkeys (e.g. (Jay and Sparks, 1984, 1987b, a; Russo and Bruce, 1994; Hartline et al., 1995; Stricanne et al., 1996; Cohen and Andersen, 2000; Groh et al., 2001; Werner-Reiss et al., 2003; Fu et al., 2004; Zwiers et al., 2004; Mullette-Gillman et al., 2005; Porter et al., 2006; Mullette-Gillman et al., 2009; Maier and Groh, 2010; Bulkin and Groh, 2012a, b; Lee and Groh, 2012; Willett et al., 2019; Caruso et al., 2021); (See also: (Zella et al., 2001; Populin et al., 2004). The discovery of EMREOs in both humans and monkeys (Gruters et al., 2018; Murphy et al., 2020; Lovich et al., 2022; King et al., submitted) afforded an opportunity to study an early aspect of this process in the same way in two different species. Given that how EMREOs actually contribute to auditory coordinate transformations has not yet been established, a comparison between human and

monkey EMREOs provides an opportunity to identify clues as to which aspects of the EMREO signal are conserved across species.

We report here that in both humans and monkeys, EMREO waveforms depend on the magnitude and direction of the accompanying saccade, especially in the horizontal dimension. Performance of a visual task is not necessary; the signal is similar regardless of whether there is an explicit reason for making a saccade or if the participant is free-viewing. EMREOs occur without the presentation of visual or auditory stimuli and across an assortment of target locations, saccade magnitudes, and saccade tasks. The EMREO's dependence on horizontal eye displacement differs only in frequency across humans and monkeys, which may be attributed to the speed at which monkeys make eye movements. This association between EMREO waveform and saccade speed, together with the robustness of the findings across saccade tasks, provide circumstantial support to the theory that the source of this signal is a corollary discharge signal related to eye movements. Alternatively, differences in the resonance properties of the eardrum or associated structures could also contribute to these frequency/shape differences.

In contrast to the largely similar horizontal displacement component, the waveform of the constant component in the EMREO regression analysis differed across humans and monkeys. The constant term reflects the average EMREO waveform across all directions and amplitudes of movement. In humans, there appears to be a basic non-zero EMREO waveform upon which the dependence on eye movement parameters is superimposed. In monkeys, this basic EMREO waveform is much smaller, leaving chiefly the dependence of the waveform on the eye movement parameters as the dominant signal. That the basic EMREO waveform is different between humans and monkeys, despite largely similar visual-auditory-oculomotor constraints and performance in the two species, suggests that the overall shape of the EMREO waveform may be of less significance than its dependence on eye movement parameters.

Our study provides an advance over our previous work (Gruters et al., 2018) in several ways. Our previous study presented monkey data in aggregate only, and while the results appeared qualitatively similar to the aggregated human data, we did not perform a quantitative analysis of the monkey data to establish that parallel on a more formal basis. Here, we used the same regression analysis on both human and monkey data, and we evaluated the pattern of results at both the individual and population levels. We also focused on both the dependence of

the EMREO on the horizontal displacement of the eyes and the average EMREO waveform for comparison purposes.

Our study has several limitations. The free-viewing method did not permit fully exploring aspects of the EMREO signal relating to the initial position of the eyes or whether a dependence on the vertical dimension of eye movements might be similar in humans vs monkeys. Future work with a controlled task will be needed to clarify these points. A second related limitation of both the current work and our previous work is that the use of a microphone to measure the efferent system of the ear limits the analysis to oscillatory aspects of the signal; it is possible that there are steady state changes that are not reflected in the measurements made here. Such steady state changes can potentially be detected via laser doppler vibrometry or optical coherence tomography (Starovoyt et al., 2019) and may provide more information about sensitivity to initial/final eye position.

A third limitation is that we did not attempt to quantify the overall amplitude of the EMREO in humans vs. monkeys. This would have been challenging for several reasons. The microphone used here is specialized for the frequency range of conventional otacoustic emissions (e.g. > 300 Hz), and thus its gain in the much lower frequency range of EMREOs is less certain (we have previously estimated that the amplitude of the human EMREO for an 18 degree eye movement to be about 57 dB SPL, based on modeling of the microphone's transfer function in this frequency range (Gruters et al., 2018). Second, the relationship between the microphone's output and the amplitude of the eardrum oscillation will depend on the size and acoustic properties of the ear canal space, which likely differ between humans and monkeys. Accordingly, the microphone measurements used in this study are expressed in units of standard deviation relative to a baseline period. This permits comparison across species on an even footing, although it leaves uncertain the precise conversion to sound pressure level.

Our overarching theory is that the mechanism(s) underlying EMREOs contribute to the process of localizing an incoming sound with respect to the eyes. How exactly this may happen remains uncertain. The cues to sound location involve interaural timing differences, interaural level differences, and the spectral content of sound. Eye-movement-related adjustments to any

of these cues could contribute to the computation of sound location with respect to the eyes for subsequent integration with visual signals.

Understanding how this might occur requires considering the potential role(s) of the ear's motor elements in generating EMREOs. These candidate motor elements consist of the two middle ear muscles (MEMs), the stapedius and tensor tympani, and the outer hair cells (OHCs). Generally, all three of these motor elements are thought to control the gain of the response of the ear to sound, with the MEMs thought of as playing a role in dampening the responses to loud sounds and the OHCs thought of as enhancing the responses to quiet sounds. Adjusting the gain of the response *differently* in the two ears in an eye movement dependent fashion would likely affect the inferred interaural level difference cues. In addition, recent work by (Cho et al., in press) has suggested that contractions of the middle ear muscles should not only influence the gain of responsiveness to incoming sound, but also the time delay of sound transmission, and thus potentially interaural timing difference cues. Both timing and level difference cues relate solely to the horizontal dimension, which is the most powerful contributor to the EMREO signal in both humans and monkeys. How spectral cues are processed in the brain is less well known, but the ability of OHCs to alter processing in a frequency specific fashion could be relevant to how this cue might be modulated in an eye movement dependent way.

Candidate anatomical pathways by which oculomotor commands could reach any or all of these actuators exist. For example, the superior colliculus, a brain region involved in controlling eye movements, projects to the inferior colliculus (IC), an auditory structure (Coleman and Clerici, 1987; Sparks and Hartwich-Young, 1989). Auditory signals in both the SC and the IC are sensitive to changes in eye position (SC: (Jay and Sparks, 1984, 1987b, a; Hartline et al., 1995; Zella et al., 2001; Populin et al., 2004; Lee and Groh, 2012) ; IC: (Groh et al., 2001; Zwiers et al., 2004; Porter et al., 2006; Bulkin and Groh, 2012b, a; Willett et al., 2019), and the IC conveys descending projections to both the superior olivary complex (Faye-Lund, 1986), the source of descending input to the outer hair cells (Guinan, 2006; Ciuman, 2010) and the cochlear nucleus (Milinkeviciute et al., 2017; Balmer and Trussell, 2022) which in turn projects to the facial and trigeminal nerves that innervate the stapedius and tensor tympani respectively (Mukerji et al., 2010). Preliminary findings from our group are consistent with a role for all three of these types of motor actuators in the generation of EMREOs (King et al., 2023). Further study regarding these motor components and how they control mechanical

processes in the ear will benefit from an animal model with a significant and consistent EMREO and with comparable ear anatomy to humans. With an animal model similar enough to humans, interventional studies can be conducted to isolate the source of motor commands and their impact on the motor actuators that create and/ or modulate the EMREO signal.

Overall, it is important to understand the similarities and differences of the EMREO signal across species when considering future work to determine which anatomical components are necessary and functional in the EMREO signal. With information about the key features that are conserved in the signal, we can answer questions about the physical mechanisms in the ear that generate the EMREO and lead to sound localization and, eventually, perception.

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