

ORIGINAL ARTICLE

Action-locked Neural Responses in Auditory Cortex to Self-generated Sounds

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Abstract

Sensory perception is a product of interactions between the internal state of an organism and the physical attributes of a stimulus. It has been shown across the animal kingdom that perception and sensory-evoked physiological responses are modulated depending on whether or not the stimulus is the consequence of voluntary actions. These phenomena are often attributed to motor signals sent to relevant sensory regions that convey information about upcoming sensory consequences. However, the neurophysiological signature of action-locked modulations in sensory cortex, and their relationship with perception, is still unclear. In the current study, we recorded neurophysiological (using Magnetoencephalography) and behavioral responses from 16 healthy subjects performing an auditory detection task of faint tones. Tones were either generated by subjects' voluntary button presses or occurred predictably following a visual cue. By introducing a constant temporal delay between button press/cue and tone delivery, and applying source-level analysis, we decoupled action-locked and auditory-locked activity in auditory cortex. We show action-locked evoked-responses in auditory cortex following sound-triggering actions and preceding sound onset. Such evoked-responses were not found for button-presses that were not coupled with sounds, or sounds delivered following a predictive visual cue. Our results provide evidence for efferent signals in human auditory cortex that are locked to voluntary actions coupled with future auditory consequences.

Key words: auditory perception, MEG, motor-sensory interactions, voluntary actions

Introduction

Voluntary actions are commonly coupled with sensory consequences—such as the sound of our footsteps during walking, or the tactile feedback when typing on a computer. Previous studies have demonstrated that perception of sensory stimuli is modulated, depending on whether they are produced through voluntary actions of the perceiver or by an external source (Crapse and Sommer 2008a, 2008b; Hughes and Waszak 2011; Reznik and Mukamel 2018). For example, in the auditory domain, perceived loudness is typically attenuated for salient self-generated sounds compared to identical sounds produced by someone else (e.g., Weiss et al. 2011). Similarly, perceived

tactile pressure is lower when it is applied by the perceiver versus by an external source (Blakemore et al. 1998; Shergill et al. 2005; Walsh et al. 2011; Kilteni and Ehrsson 2020), an effect also associated with the phenomenon that one cannot tickle oneself (Blakemore et al. 1999).

A common explanation for these phenomena at the neural level, proposed in the early 1950s, is that during voluntary execution of actions, the motor system sends an “efference copy” (Von Holst 1954) conveying the expected sensory outcome to relevant sensory cortex. This signal results in a local “corollary discharge” (Sperry 1950), that changes the neural state of the sensory system. Since these early studies, the role of

action-induced modulation of neural activity in sensory regions during action generation, as well as its role in perceptual modulations, has been extensively studied in rodents, non-human primates and humans across various tasks and modalities, including auditory, visual, and tactile (Eliades and Wang 2003; Crapse and Sommer 2008a, 2008b; Lee and Middlebrooks 2011; Saleem et al. 2013; Morillon et al. 2016; Reznik and Mukamel 2018; van Kemenade et al. 2019). The results of these studies suggest that voluntary actions play an important role in perception, by directly modulating neural activity in sensory circuits.

In the auditory domain, sound-triggering actions have been shown to modulate auditory evoked responses in humans. The magnitude of the N100/M100 component of the EEG/MEG sound-evoked response is typically attenuated when sounds are actively generated by the perceiver relative to the response evoked by identical sounds from an external source (Baess et al. 2011; Weiss et al. 2011; Nelson et al. 2013; Buran et al. 2014; Morillon et al. 2014; Schneider et al. 2014; Zhou et al. 2014; Horvath 2015). However, since in most paradigms the sound is usually presented immediately following the generating action (e.g., button press), when measuring the modulated sound-evoked signal it is difficult to disambiguate the relative contribution of action-related signals from bottom-up sensory signals evoked by the stimulus.

In the current study, we examined how sound-eliciting button presses affect 1) the neural state in auditory cortex preceding sound onset and 2) the perception of sounds presented at auditory hearing threshold. To this end, subjects performed a sound detection task of faint auditory stimuli, that were physically identical but either self-generated (active condition via button presses) or generated by the computer (passive condition). Critically, in the active condition, we introduced a constant temporal delay between the action and its auditory outcome in order to decouple top-down, action-locked neural evoked-responses from bottom-up sound-evoked responses in auditory cortex. Neural activity was measured using Magnetoencephalography (MEG) and analyzed in source space, further allowing us to distinguish between neural responses in motor and auditory cortices. Our results show increased perception of self-generated sounds, together with action-locked neural responses in auditory cortex preceding sound-onset that depend on the coupling between the action and auditory consequences.

Materials and Methods

Participants

Eighteen participants naïve to the purpose of the experiment were recruited to this study. Two participants did not complete the experimental procedure (one participant withdrew from the experiment and the other participant was interrupted by a fire alarm in the MEG facility), yielding a total of 16 participants (11 females; mean age—22.9, range—19–27 years) for subsequent analyses. All participants reported right hand dominance and normal vision and hearing. The study was approved by the Ethics committee of Bar-Ilan University and the Ethics committee of Tel-Aviv University. All participants provided written informed consent to participate in the study and were compensated for their time.

Procedure and Stimuli

Prior to the experimental task, we assessed individual participants' auditory detection thresholds for binaural delivery of pure tones (pitch: 1 kHz, duration: 300 ms including linear

rise/decay time of 25 ms using a '1 step up, 2 steps down' staircase procedure (Gelfand 2010); 1 dB step size). On each trial, participants pressed a button with their right index finger that triggered the presentation of a tone. Participants indicated whether or not they heard it by pressing one of two buttons using their left hand. If a sound was detected, sound pressure level (SPL) on the next trial was lowered by 2 dB and if not, SPL on the next trial was increased by 1 dB. The lowest intensity at which a subject reported detection twice (once going up and once going down) was determined as the auditory detection threshold (Gelfand 2010). The sound-intensity corresponding to each individual's auditory detection threshold was used throughout the main experiment described next.

The main experiment was an auditory detection task comprised of active and passive experimental conditions (Fig. 1). In the active condition, participants saw a visual cue ("+" on a black screen) signaling the beginning of the trial. Once a trial was initiated, subjects were allowed to press a button with their right index finger "at their own time" (no time limit was imposed). In 50% of the trials, the near-threshold sound was presented 500 ms after the button press, whereas in the remaining trials no sound was delivered. Similarly, in the passive condition, the same visual cue was presented on the screen, but instead of cueing the subject to press the button, it indicated that a sound might be presented 500 ms later (sounds occurred in 50% of the trials, similar to the active condition). In both conditions, participants were asked to report whether or not they heard a sound via button press using their left hand (index/middle finger; the mapping of "yes/no" detection responses to specific fingers was randomized in each trial to avoid motor preparation). The order of sound/no sound trials was randomly mixed within each block. This design allowed us to measure the hit and false alarm rates and to calculate the sensitivity (d') and criterion (c) measures (Green and Swets 1974), for both active and passive conditions. During the inter-trial-interval (randomly varied between 1.5 and 2.5 s), a blank black screen was shown. The conditions were presented in 30 randomized blocks (total of 15 active and 15 passive blocks), each one consisting of 10 trials (Reznik et al. 2014). Before each block, participants were visually informed about the upcoming condition type by the words "ACTIVE" or "PASSIVE" appearing on the screen. Each block started by the subject pressing a button with their left hand.

To allow functional source localization (see below), following the main auditory detection task, participants underwent an auditory localizer task in which they passively listened to 75 salient pure tones (300 ms, 1 kHz) delivered binaurally with random inter-stimulus-interval ranging from 1.5 to 2.5 s.

Finally, to measure activity in auditory cortex associated with button presses that are not associated with auditory outcome (i.e., without sound delivery), subjects performed a silent motor task ('motor-only') in which they were prompted by a visual cue ("+" on a black screen) to spontaneously perform a single button press with their right index finger. This task is similar to the active condition blocks; however, the subjects were explicitly informed that their actions are no longer associated with sound delivery.

MEG Recording

During the experimental sessions, participants laid in a supine position in a magnetically shielded room while brain activity was recorded using a whole head 248-channel magnetometer array (4-D Neuroimaging, Magnes 3600 WH) located at Gonda

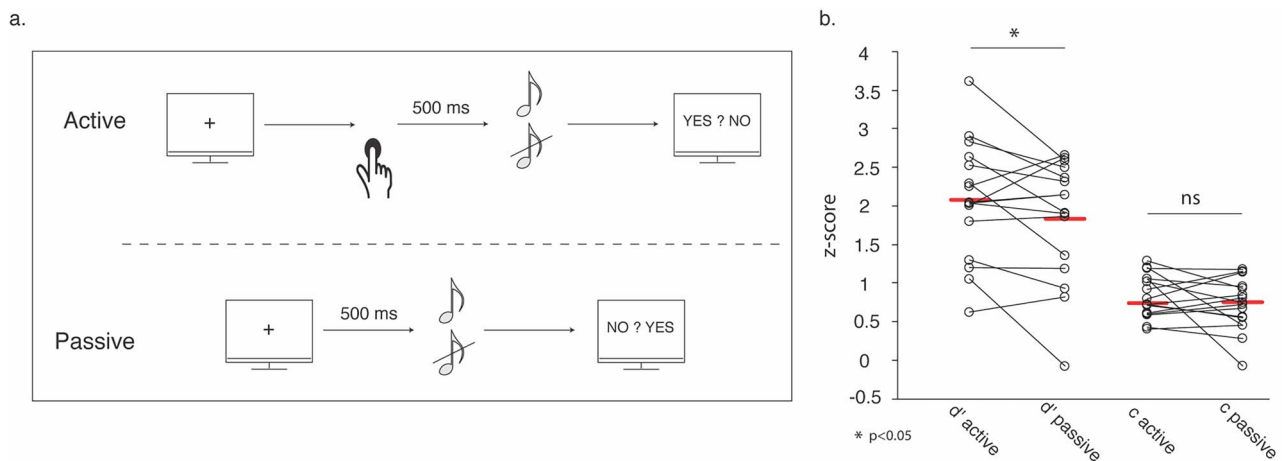


Figure 1. Experimental design and performance in the auditory detection task. (a) In the active condition, the appearance of a visual cue (“+”) indicated the beginning of the trial and subjects pressed the button with their right index finger at their own time. 500 ms following the button press a pure tone was delivered in 50% of the trials. In the passive condition, a pure tone was delivered in 50% of the trials 500 ms following the appearance of the visual cue. At the end of each trial, subjects answered whether they heard the tone by pressing a button with their left hand. Tones were delivered at individual subjects’ auditory detection levels. (b) Individual subject performance ($n = 16$) in the auditory detection task. Group means are shown with red lines and individual subjects are shown with dots connected across conditions. While subjects’ auditory sensitivity (measured with d') was greater in the active compared with passive conditions, subjects’ criterion did not differ between the two conditions.

Brain Research Center in Bar-Ilan University. Neuromagnetic activity was measured with a sampling rate of 1017.23 Hz and filtered online using 0.1–400 Hz band-pass filter. Five magnetic coils were attached to participants’ scalp to track the position of their head relative to the magnetometer array. The locations of the coils were determined with respect to 3 anatomical landmarks—nasion and left and right mastoid points. The head shape of each participant was digitized using a digital stylus (Polhemus). Sounds were delivered from a computer via Roland Octa Capture sound card through MEG-compatible in-ear earphones (Etymotic Research ER30). Subject button presses were registered using an MEG-compatible responses box (Current Designs Finger Tapper).

MEG Pre-processing

MEG data were preprocessed using MNE toolbox for python (Gramfort et al. 2013). External noises (power-line, mechanical vibrations of the building) were removed offline using a pre-designed algorithm (Tal and Abeles 2013). A single noisy channel was excluded from analysis based on visual inspection, and signal associated with heart beats was removed using signal space projection algorithm (Uusitalo and Ilmoniemi 1997). Trials were rejected based on peak-to-peak amplitude (threshold = $4.5e-12$ FT). Data from the main experiment were segmented into 2 s-long epochs—from 1 s before sound onset until 1 s after sound onset. In the motor and auditory localizer tasks, data were similarly segmented into 2 s epochs—spanning 1 s before and after the sound onset, and 1 s before to 1 s after the press. Each trial was baseline corrected for its own global mean and the average response was calculated for each condition and each subject. Since the number of trials across conditions was not identical (due to differences in the number of detected/not-detected trials, and discarded trials following signal pre-processing) and since MNE dynamic statistical parametric mapping (dSPM) is sensitive to the number of trials used for the averaged signal, for each comparison, we equated the number of trials within each subject across conditions by

randomly selecting trials from the conditions with higher number of trials. For example, when comparing MEG signal in active hit versus miss trials, the number of trials for each condition was equated within each subject by random sampling of trials from the condition with more trials. This random sampling was repeated 100 times in each subject and the average source-projected signal was taken across all iterations.

MEG Source Localization

For each participant, we fitted the digitized head shape to a template MRI model, allowing a common source space for grand averaging across participants. MNE dynamic statistical parametric mapping was used to project MEG data from the sensor space to the cortical surface template. This resulted in 10 242 source reconstructed MEG signals (i.e., vertices) per hemisphere. Empirical estimate of the noise covariance was calculated from the pre-stimulus period in the auditory localizer task (200 ms window prior to sound onset), using an automated model selection procedure (Engemann and Gramfort 2015). We used a boundary-element model (BEM) method to model activity at each vertex and calculate a forward solution. An inverse solution was estimated using this forward model and the noise estimate (SNR = 1).

MEG Data Analysis

We defined three Regions of interest (ROI)—right and left auditory cortex, and left somatomotor cortex. The somatomotor ROI was identified based on activity between 100–200 ms after button press in the active and motor-only conditions (see cortical maps in Fig. 3 and the blue contour in Fig. 4). We used data from both conditions in order not to bias our selection of vertices when examining differences between these two conditions in left somatomotor cortex. Auditory ROIs were identified based on activity in a 300-ms long window following tone presentation in the auditory localizer task. ROIs (auditory and motor) were defined as all vertices in a radius of 5 mm around the top 0.5% of active vertices in the above mentioned time-windows. When

applicable, *P*-values were Bonferroni corrected for multiple comparisons.

Results

Behavioral Data

After assessing individual auditory hearing thresholds, each subject was engaged in a sound-detection task in which faint sounds were presented on 50% of the trials (see Methods and Fig. 1a). The mean proportion of detected sounds across subjects was 0.58 ± 0.04 on trials in which sounds were presented (hits). In agreement with our previous reports (Reznik et al. 2014; Reznik, Henkin, et al. 2015a), participants showed increased sensitivity to sounds in the active compared to passive condition (mean \pm SEM d' across subjects: active $d' = 2.07 \pm 0.19$, Passive $d' = 1.82 \pm 0.19$; paired *t*-test, $t_{(15)} = 2.28$, $P = 0.03$; see Fig. 1b for group and individual subjects data). Importantly, participants showed no difference in bias for responding “yes” versus “no” regarding sound detection across conditions (mean \pm SEM c across subjects: active $c = 0.74 \pm 0.05$, passive $c = 0.75 \pm 0.06$; paired *t*-test, $t_{(15)} = 0.13$, $P = 0.89$; Fig. 1b). In the active condition, we did not impose a temporal limit between the appearance of the visual cue and subjects’ button presses. On average, subjects pressed the button 936 ms following presentation of the visual cue and no significant difference was found between response times in subsequently detected versus non-detected (hit vs. miss) trials (mean \pm SEM response time across subjects: active-hit: 907 ± 4 ms, active-miss: 1001 ± 6 ms; *t*-test on log-transformed response time, $t_{(15)} = 1.61$, $P = 0.13$). In addition to the active and passive conditions, subjects also performed a motor-only task in which they pressed buttons with no auditory consequences (see Methods). In this task, subjects pressed the button on average 582 ± 59 ms following the visual cue, which was shorter than the time they waited between visual cue and voluntary presses in the active trials ($n = 14$; due to technical reasons response times in this condition were not obtained in 2 subjects; *t*-test on log-transformed response time, $t_{(13)} = 5.82$, $P < 0.001$).

Sound-evoked Neural Activity in Auditory Cortex

The sound-evoked response in auditory cortex to the threshold-level sounds showed a peak around 230 ms following sound onset in the active and passive conditions (mean across participants, conditions, and hemispheres). We averaged the response in a 100-ms window centered around the peak response from each participant and condition, and compared the magnitude of the auditory evoked responses in active and passive conditions collapsed across hemispheres. In line with previous reports of sensory attenuation, we found attenuated auditory responses in the active condition (mean \pm SEM dSPM across subjects—active: 1.77 ± 0.13 ; passive: 2.13 ± 0.22 ; paired *t*-test, $t_{(15)} = 2.34$, $P = 0.03$). Note that in our paradigm, sounds in about half of the trials were not perceived (as opposed to previous literature reporting sensory attenuation using supra-threshold sounds). Therefore, in order to isolate any potential effect of subjective perception, we also compared auditory-evoked responses across active/passive conditions only in the hit trials, in which participants reported they heard the delivered sound. When restricting the analysis only to these trials, we still find attenuated auditory-evoked responses in the active condition (mean \pm SEM dSPM across subjects—active

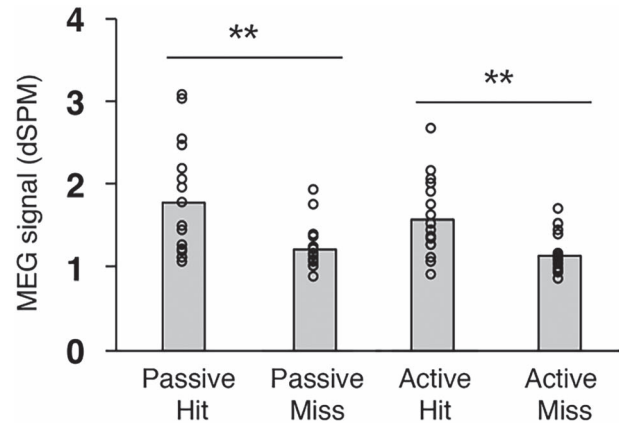


Figure 2. Sound-evoked activity in auditory cortex. Group-level ($n = 16$) comparisons of sound-evoked activity in right and left auditory cortex. Sound-evoked activity in auditory cortex was greater in both active and passive conditions on trials in which subjects successfully detected the auditory tones (hit trials) compared with trials in which they failed to do so (miss trials).

hit: 1.56 ± 0.11 ; passive hit: 1.78 ± 0.17 , $t_{(15)} = 2.47$, $P = 0.025$). In miss trials, where participants reported they did not hear the delivered sound, no significant difference was found (mean \pm SEM dSPM across subjects—active miss: 1.13 ± 0.05 ; passive miss: 1.21 ± 0.06 , $t_{(15)} = 1.44$, $P = 0.16$). Finally, we examined how the magnitude of the evoked-response to the sounds was associated with sound detection (hit vs. miss, irrespective of condition—active/passive). Comparing ‘hit’ and ‘miss’ trials, we found that sound-locked activity in auditory cortex during ‘hit’ trials was greater than the activity in ‘miss’ trials (mean \pm SEM dSPM across subjects—hit: 1.67 ± 0.13 ; miss: 1.17 ± 0.05 , $t_{(15)} = 4.43$, $P < 0.001$; Fig. 2).

Pre-sound, Neural Activity in Auditory Cortex

After establishing that self-generated faint sounds evoke attenuated responses in auditory cortex compared to identical sounds perceived in a passive manner, we further explored how motor actions modulate the neural state prior to sound onset. To this end, we compared neural activity in the active versus passive conditions during the 500 ms window following the sound-triggering button press (active condition) or visual cue indicating an upcoming sound (passive condition) and until the onset of the sound itself. This analysis focused on MEG activity in bilateral auditory cortices (left/right ROIs). We performed a 2×2 repeated measures ANOVA with the factors of Condition (active/passive) and Hemisphere (right/left auditory cortex). This 2×2 analysis revealed a main effect of Condition ($F_{(1,15)} = 15.83$; $P = 0.001$), main effect of Hemisphere ($F_{(1,15)} = 12.83$; $P = 0.003$) and a significant interaction effect ($F_{(1,15)} = 5.24$; $P = 0.037$). Post-hoc pair-wise comparisons indicated that while MEG signal was greater in the active compared with the passive conditions in the left auditory cortex (mean \pm SEM dSPM across subjects—active: 2.26 ± 0.14 , passive: 1.68 ± 0.07 , $t_{(15)} = 3.54$, $p_{\text{Bonf}} = 0.003$), no difference was observed in the right hemisphere (active: 1.57 ± 0.12 , passive: 1.46 ± 0.08 , $t_{(15)} = 0.35$, $p_{\text{Bonf}} = 0.73$; Fig. 3).

In order to confirm this selective enhancement in left auditory cortex was not due to signal leakage from motor to auditory regions, we examined whole brain (uncorrected) activation maps in the active condition 140 ms following button press (centered at the peak of the action-locked evoked response; Fig. 3).

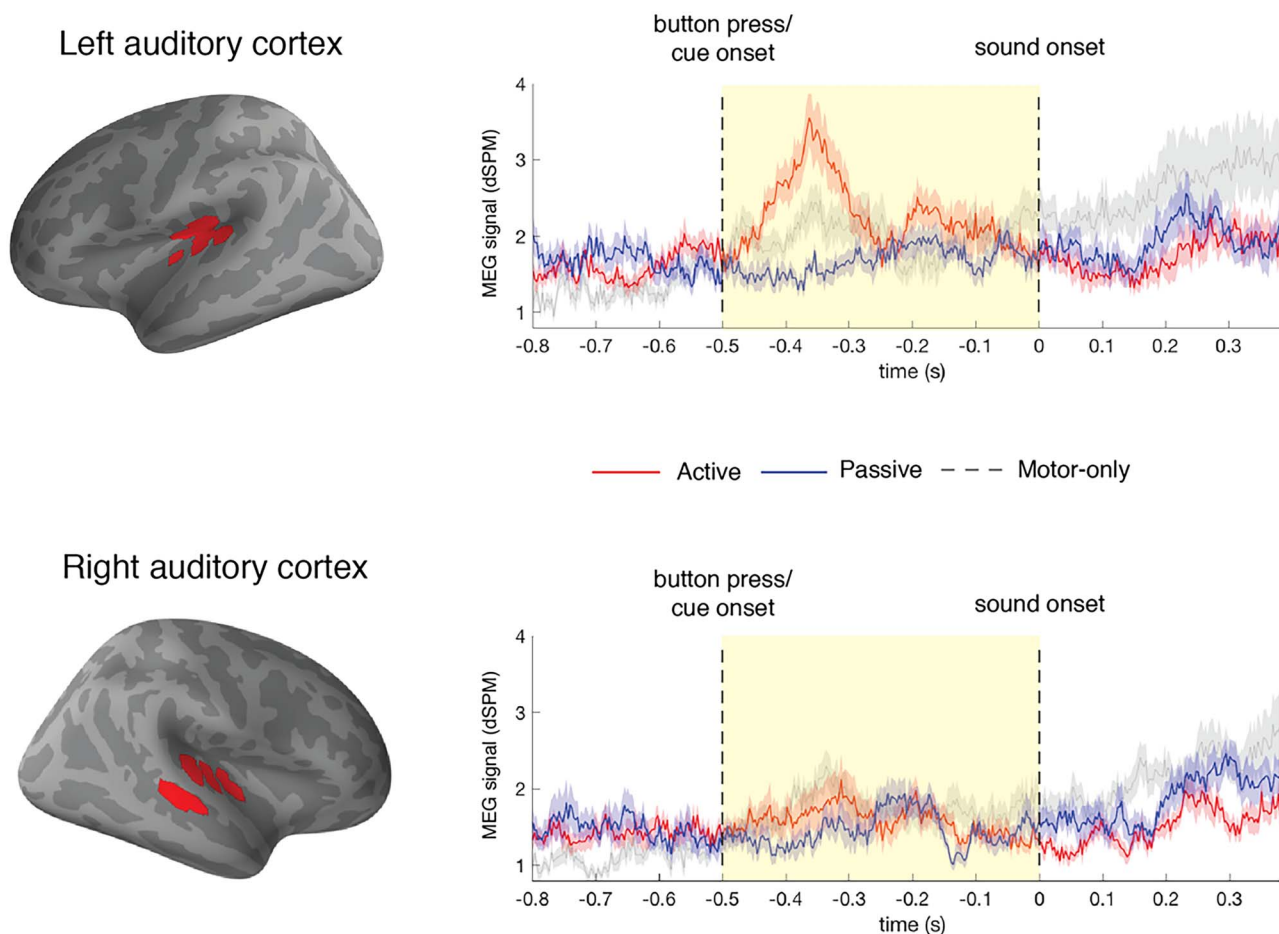


Figure 3. MEG time-course in auditory cortex during active, passive and motor-only conditions. Left panels: ROIs in left (top) and right (bottom) auditory cortex defined at the group level ($n = 16$) and projected to the cortical surface template. Right panels: group average ($n = 16$) time-courses and their SEM from the right and left auditory ROIs in the active, passive and motor-only conditions. The 500 ms time window between button press/cue onset and sound onset is marked in yellow. Note the action-locked evoked response in left auditory cortex in the active condition.

As can be seen from Figure 4, the signal in somatomotor cortex is anatomically well separated from the signal in the Sylvian fissure. Moreover, the time-courses during the active condition in left motor and auditory cortices exhibit different temporal evolution patterns (Fig. 4), while signal leakage is expected to yield similar action-locked signals. Taken together, signal leakage from motor cortex seems an unlikely explanation for the action-locked evoked responses we find in left auditory cortex in the active condition.

While the action-locked evoked-responses in the left auditory cortex are compatible with the forward-model framework, we further examined whether this activity is unique to motor-auditory association or can be explained by mere motor actions without auditory consequences. To address this issue, we compared action-locked MEG activity in left auditory cortex between the active and motor-only conditions where participants performed the same motor action, but without auditory consequences. Indeed, activity in left auditory cortex during the active condition was significantly higher than in the Motor-only condition (mean \pm SEM dSPM across subjects—active: 2.26 ± 0.14 , motor-only: 1.99 ± 0.13 , $t_{(15)} = 2.21$, $P = 0.04$; Fig. 3). Nonetheless, activity in the motor-only condition during this time-window was significantly higher than in the passive

condition ($t_{(15)} = 2.17$, $P = 0.04$), suggesting the existence of a reduced tactile/motor component in the action-locked evoked activity when button presses are not coupled to sound outcome.

Since in our experimental design the motor-only condition always followed the active condition, we examined whether the greater MEG activity in the left auditory cortex during active compared with motor-only conditions could be possibly explained by condition order. To this end, we split all trials of the active condition according to order of presentation in the experiment (first/second half) and compared the magnitude of the action-locked MEG evoked-response. No significant difference was found between the first and second half of the experiment (mean \pm SEM dSPM across subjects—1st half: 2.33 ± 0.14 , 2nd half: 2.48 ± 0.18 , $t_{(15)} = 1.32$, $P = 0.19$), compatible with the notion that condition order does not seem to play a significant role in the enhanced MEG activity we find in Active versus Motor-only conditions.

After establishing an action-related response in left auditory cortex for actions with auditory consequences, we further tested whether this response was associated with subsequent sound perception. To this end, we performed an exploratory post-hoc analysis in which we focused on the peak of action-locked evoked response during the active condition (collapsed across

Active - left hemisphere

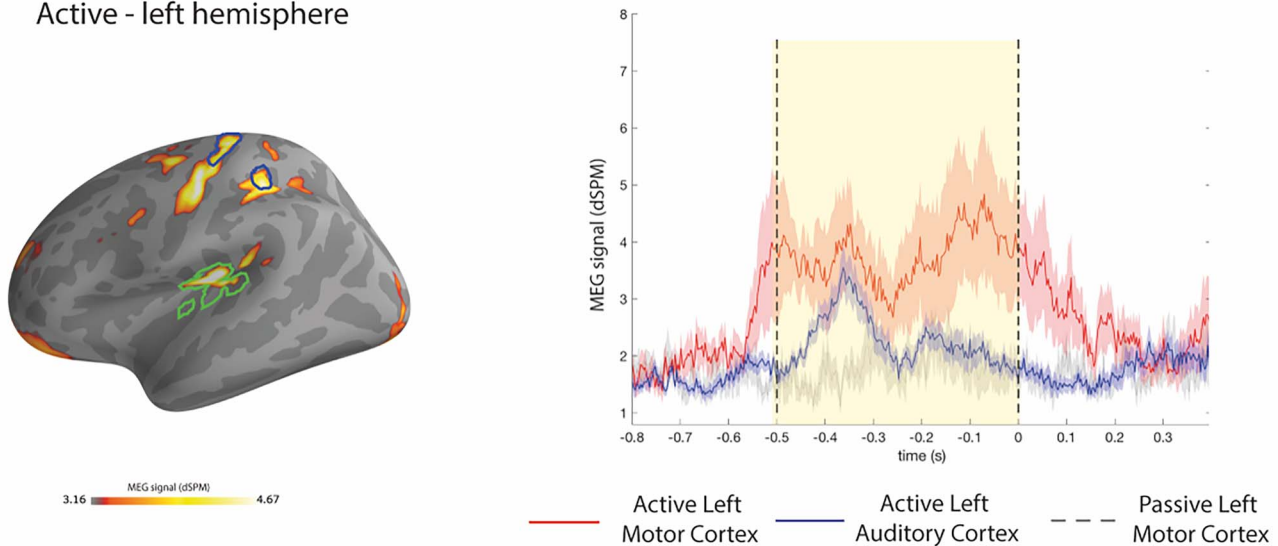


Figure 4. Somatomotor activity. Left—uncorrected activity map in the active condition (compared to baseline) around the peak response in the left auditory cortex (140 ms following button press). Note the clear anatomical separation between the motor cortex and the Sylvian fissure. Left somatomotor and auditory ROIs are marked with blue and green contours respectively. Right—group average ($n = 16$) time-courses and their SEM from the somatomotor and left auditory ROIs in the active, motor-only and passive conditions; yellow as above.

hit/miss trials). Average peak across subjects was at ~ 140 ms following the button press in the active condition (~ 360 ms prior to sound onset). We focused our analysis on a 100 ms time window around this peak. This analysis provided preliminary evidence for greater response prior to ‘hit’ compared with ‘miss’ trials in the active condition (mean \pm SEM dSPM across subjects—active hit: 2.26 ± 0.19 , active miss: 2.03 ± 0.16 , $t_{(15)} = 2.21$, $P = 0.04$; Fig. 5, yellow mark). No significant effect of subsequent performance was found in the passive condition in the corresponding time window (passive hit: 1.36 ± 0.08 , passive miss: 1.28 ± 0.05 , $t_{(15)} = 1.41$, $P = 0.18$).

Discussion

In the current study, we examined how actions that are coupled with the generation of faint auditory sounds influence auditory perception and neural activity in auditory cortex. Using MEG, we provide evidence for action-locked responses in auditory cortex contralateral to the active hand and increased perceptual salience for weak self-generated sounds.

Action-locked Neural Activity in Auditory Cortex

In most previous studies examining motor-sensory coupling, sensory consequences immediately followed the action and analysis focused on the evoked response. However, such designs do not allow assessing the independent effect that the motor actions themselves may have on neural state in auditory cortex, beyond the bottom-up sensory response (Saupe et al. 2013; Timm et al. 2013; Horvath 2015). Some studies used unexpected omission of action consequences or motor priming in order to uncover top-down motor-induced modulations that are decoupled from bottom-up, sensory evoked response (Bäz et al. 2008; SanMiguel et al. 2013; Stenner et al. 2015). In our experimental design, we decoupled actions from their sensory consequences by introducing a constant temporal delay between the

cue (motor act in the active condition and visual cue in the passive condition) and delivery of the coupled auditory consequences. Together with the high spatial and temporal resolution of MEG, this design allowed us to analyze the neural signals in auditory cortex in the time period immediately following the motor act but prior to sound-evoked responses. In left auditory cortex (contra-lateral to the hand performing the action in our experimental design) we observed a transient increase in the neural response following a button press that served as means for generating an upcoming sound. Critically, no similar increase was observed when subjects passively waited for the presentation of a sound, despite it being similarly predictable. Furthermore, these evoked responses were stronger for button presses that were associated with sounds versus silent button presses (motor-only condition). Thus, the evoked response in auditory cortex is action dependent and its magnitude depends on the association with an auditory outcome.

Interestingly, in the motor-only condition in which there was no association between actions and auditory consequences, we still find significant responses in auditory cortex preceding sound onset. Although smaller than the active condition, these responses were greater compared with the passive condition. Two non-mutually exclusive explanations can account for this result. One explanation is that the responses we observe in the motor-only condition are due to tactile feedback associated with the button press. Indeed, previous studies have shown that tactile stimulation results in evoked activity in auditory cortex (Foxe et al. 2000; Schroeder et al. 2001; Foxe et al. 2002). Another explanation is that the action-locked evoked response in auditory cortex reflects efferent activity from motor cortex during button press. Stimulation studies in rodents suggest that induced activity in motor cortex (even in lack of voluntary drive and tactile feedback) is sufficient to modulate activity in auditory cortex (Nelson et al. 2013; Schneider et al. 2014; Carcea et al. 2017). This is compatible with human studies showing that during “passive” movements (in the lack of motor cortex

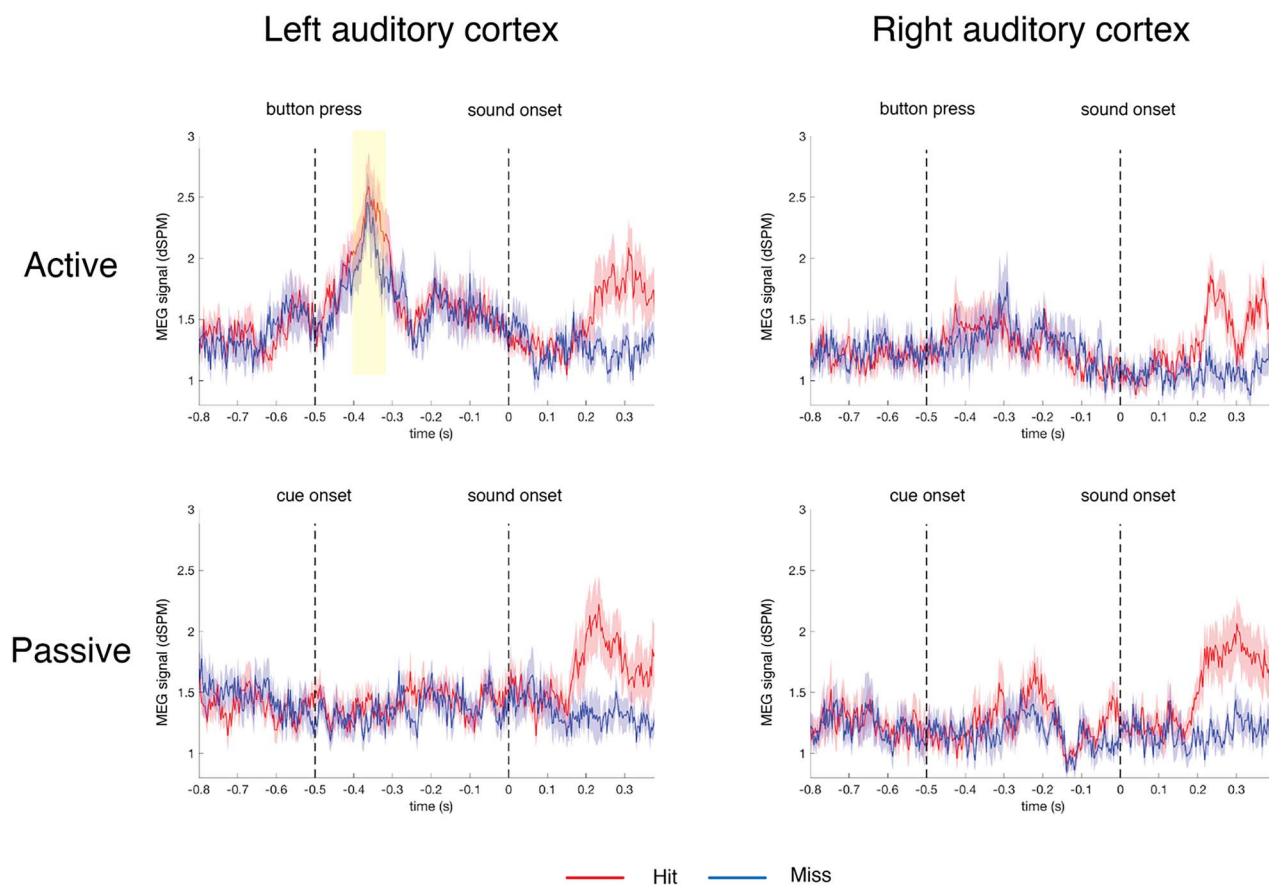


Figure 5. MEG time-course in auditory cortex during hit and miss trials in active and passive conditions. Group average ($n = 16$) time-courses and their SEM. The peak time-window in the active condition is marked in yellow.

activation; Uhlmann et al. 2020) sensory modulation effects are reduced relative to voluntary movements, supporting the added value of volition on neural modulations. At this stage, we cannot distinguish between these explanations and the role of these components awaits further study.

The action-locked increase in MEG signal we report in left auditory cortex during active sound generation was not found in right auditory cortex (ipsilateral to the button-pressing hand), suggesting a hand-dependent effect. In previous fMRI studies we found stronger modulations in auditory cortex for sounds produced with the contra-lateral hand (or ipsi-lateral to the active motor cortex; Reznik et al. 2014; Reznik, Ossmy, et al. 2015b). In addition, we recently reported that fMRI signals in visual cortex are differentially modulated according to the hand (right/left) that was used to elicit the visual stimulus (Buaron et al. 2020). For more evidence showing motor-induced modulation of visual neural and behavioral processing see, for example, Bennett et al. 2013; Desantis et al. 2014. Although in the current study we did not have a left-hand sound triggering condition, current MEG data further support the notion that modulations in sensory regions have a component of limb-specificity.

Sound-evoked Neural Activity in Auditory Cortex

With respect to sound-evoked neural responses in auditory cortex, we find attenuated neural activity in response to

self-generated sounds compared with identical sounds perceived in a passive manner. These results are compatible with the literature reporting attenuated neural activity to self-generated action consequences (Baess et al. 2011; Horvath 2015), extending this phenomenon also to faint sounds. Furthermore, we find correspondence between perception (hit/miss) and magnitude of the evoked responses. Since we used faint sounds with fixed amplitude at the subject's hearing threshold, their detection varied across trials. We find that sound-evoked responses in trials in which the sound was perceived (hit trials) were stronger than the sound-evoked responses of trials in which sounds were not detected (miss trials). These results are in agreement with previous studies reporting physiological correlations with behavior (Hillyard et al. 1971; Jones et al. 2007). We note that auditory feedback in our study was discrete (single auditory tones). Recent studies comparing discrete and continuous (more naturalistic) feedback report stronger suppression of fMRI signal in the continuous case (van Kemenade et al. 2019; Uhlmann et al. 2020). The mechanism giving rise to such differences needs further investigation.

With respect to time-to-peak of the evoked response, we note that in our current results it was late (~ 230 ms) relative to typical auditory evoked responses (~ 100 ms). This is probably due to the use of faint near-threshold sounds, which are known to elicit prolonged and reduced evoked responses (Neukirch et al. 2002). Another possibility is that M100 component was too small to be detected and the observed auditory-evoked activity we report

actually reflects the MEG equivalent of EEG N200-family signals (Folstein and Van Petten 2008).

Perceptual Enhancement of Faint Self-generated Sounds

Consistent with our previous reports (Reznik et al. 2014; Reznik, Henkin, et al. 2015a), we find increased perceptual sensitivity in the active versus passive condition. Our experimental design provides important information with respect to the temporal window in which action-induced modulations affect perception. In the tactile domain, behavioral results show that a delay of ~300 ms between the action and tactile consequences abolishes perceptual attenuation (Blakemore et al. 1999; Bays et al. 2005). In the auditory domain, the amplitude of the N100 component is still attenuated when sounds were delivered with 500–1000 ms delay following sound triggering actions (Bäß et al. 2008). We find that perceptual modulations and neural attenuation for self-generated sounds are maintained with a temporal delay of 500 ms. In our study, subjects were explicitly informed about the 500 ms delay between the button press and sound delivery. Despite this long delay, we still observed neural and behavioral modulations of auditory processing, similar to modulations reported in studies with immediate auditory feedback (e.g., Reznik et al. 2014; Reznik, Henkin, et al. 2015a). However, since the action-sound contingency was fixed in all conditions, our ability to ascribe motor-locked responses in auditory cortex to differences in the degree of predictability is limited. The effects of long delays and differences in levels of predictability on motor-sensory recalibration and sense of agentic control still requires further research (Haggard 2017; Press et al. 2020; Arian et al. 2021).

It is important to note, that since in the active condition participants had a visual cue to perform the sound-triggering action, there was potentially more time to prepare for the upcoming auditory stimuli compared with the passive condition where participants only had the visual cue period. Therefore, the perceptual enhancement we observe in the active condition could be, in principle, attributed to non-action-specific differences (Kok et al. 2017). One possible way to address this issue in future studies is to replace the action in the active condition with another sensory cue.

Another non-motor-specific explanation to the enhanced sound detection in the active condition is differences in attentional demands placed on the participants compared with the passive condition. However, previous studies demonstrated that modulated responses to self-generated sounds were not affected by attentional allocation (Saupe et al. 2013; Timm et al. 2013; Schroger et al. 2015). Another, yet related, possible explanation to our behavioral and physiological findings is differences in temporal expectation across conditions that has been shown to modulate perceptual decision making (Kok et al. 2012; Summerfield and de Lange 2014). Previous studies suggest that motor activity provides predictive information about the temporal onset of self-generated stimuli, thus making them inherently more predictable compared with stimuli triggered by an external source (Hughes et al. 2013; Morillon et al. 2016). However, modulated auditory activity in response to self-generated sounds was reported irrespective of differences in temporal prediction (Ford et al. 2007; Bäß et al. 2008; Lange 2011; Oestreich et al. 2015). Although we cannot completely rule out these differences, by introducing a constant

temporal delay between cue (passive condition)/button-press (active condition) and sound onset, we believe our experimental design reduces potential differences in temporal expectation levels of sound onset across active and passive conditions.

The Association between Sound Detection and Neural States in Auditory Cortex

In the human literature, the term sensory attenuation has been used to describe both the behavioral phenomenon of reduced perception (e.g., level of ticklishness, or sound loudness), and the physiological phenomenon of decreased evoked responses measured by EEG or MEG (N100 or M100, respectively). However, to date, there is no causal evidence linking the two phenomena. Moreover, a recent study by Palmer and colleagues even suggests different underlying mechanisms (Palmer et al. 2016).

Our behavioral results point to enhanced sensitivity to self-generated sounds. At the physiological level, we examined both action-locked and sound-locked activity in auditory cortex. Our exploratory analysis of action-locked activity in auditory cortex demonstrates that the amplitude of the evoked response corresponds with subsequent sound detection. Although still exploratory at this stage, these results suggest that action-induced neural modulations in auditory cortex may play a role in the behavioral manifestation of sensory modulations. The causal link between such motor-evoked physiological markers in auditory cortex and behavioral reports requires further studies.

Our sound-locked neural results point to attenuated auditory evoked responses in the active compared with passive conditions. This neurophysiological finding of sensory attenuation seems to contradict the behavioral finding of sensory enhancement. However, animal studies show that motor output results in 1) global inhibition of both evoked and spontaneous activity in auditory cortex (Nelson et al. 2013; Schneider et al. 2014; Schneider et al. 2018) and 2) increase in neural signal-to-noise ratio that can be reflected in enhanced detection of weak self-generated action consequences at the behavioral level (Buran et al. 2014; Zhou et al. 2014; Carcea et al. 2017; Reznik and Mukamel 2018). Together, these two phenomena may explain our seemingly contradicting behavioral and physiological findings.

In summary, we show action-locked responses in auditory cortex contralateral to the active hand and increased perceptual salience of faint auditory stimuli compared to otherwise identical sounds perceived in a passive manner. Our results constitute an important step in understanding the neural mechanisms of top-down modulations during perception of self-generated action consequences.

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