

Immersive audiomotor game play enhances neural and perceptual salience of weak signals in noise

Jonathon P. Whitton^{a,b,1}, Kenneth E. Hancock^{a,c}, and Daniel B. Polley^{a,c,1}

^aEaton-Peabody Laboratories, Massachusetts Eye and Ear Infirmary, Boston, MA 02114; ^bProgram in Speech Hearing Bioscience and Technology, Harvard–Massachusetts Institute of Technology Division of Health, Sciences, and Technology, Cambridge, MA 02139; and ^cDepartment of Otolaryngology, Harvard Medical School, Boston, MA 02115

Edited by Nancy J. Kopell, Boston University, Boston, MA, and approved May 13, 2014 (received for review December 3, 2013)

All sensory systems face the fundamental challenge of encoding weak signals in noisy backgrounds. Although discrimination abilities can improve with practice, these benefits rarely generalize to untrained stimulus dimensions. Inspired by recent findings that action video game training can impart a broader spectrum of benefits than traditional perceptual learning paradigms, we trained adult humans and mice in an immersive audio game that challenged them to forage for hidden auditory targets in a 2D soundscape. Both species learned to modulate their angular search vectors and target approach velocities based on real-time changes in the level of a weak tone embedded in broadband noise. In humans, mastery of this tone in noise task generalized to an improved ability to comprehend spoken sentences in speech babble noise. Neural plasticity in the auditory cortex of trained mice supported improved decoding of low-intensity sounds at the training frequency and an enhanced resistance to interference from background masking noise. These findings highlight the potential to improve the neural and perceptual salience of degraded sensory stimuli through immersive computerized games.

foraging | hearing | cortical | gradient search | noise suppression

Efficient search for resources is critical to the survival of most species. As such, foraging represents a conserved, adaptive behavior that drives decision making under the types of naturalistic contexts for which brains have evolved. Efficient foraging involves the dynamic integration of sensory cues, memory, and the costs and values associated with foraging decisions (1–3). The sensory cues used to guide foraging can be either discrete or gradient-based. For instance, moths, dogs, and humans navigate odor gradients using characteristic casting and zigzagging behaviors in response to dynamic somatosensory and olfactory cues (4–6). Although the successful execution of these behaviors would be expected to strongly rely on the integration of rapidly changing, weak and noisy sensory information, previous work has primarily focused on computations involved in cost/value decisions related to the exploration/exploitation trade-off (1, 2, 7–9), rather than whether and how foraging behavior is refined through learned associations between these dynamic sensory cues and reinforcement signals (but see refs. 10–12).

Accumulating evidence suggests that sensory learning in mature animals reflects the coordinated activation of sensory brain areas and neuromodulatory control nuclei (13). Of these neuromodulatory systems, cholinergic and dopaminergic neurons in the nucleus basalis and ventral tegmental area, respectively, have been observed to code cognitive operations of cue detection (14, 15) and reward prediction (16) associated with behaviorally relevant sensory stimuli and to subservise learning in complex sensory-guided tasks (17). Theoretically, these learning systems are maximally engaged by tasks that require the continuous interplay of sensory cues, dynamically updated motor action programs, and neuromodulatory feedback as occurs during the naturalistic process of sensory-guided foraging. This “closed-loop” approach to perceptual training has very little in common with traditional perceptual learning studies, wherein isolated and

unpredictable stimuli are presented at low rates with sparse, temporally distant feedback signals, and training improvements typically do not generalize beyond the specific practice materials. By contrast, sensory-guided foraging shares many characteristics with exploration-based, immersive sensorimotor learning tasks such as musical training (18, 19) and action video game play (20–22), which appear to promote highly generalizable improvements in sensory perception (18, 20, 21). Training protocols that engage learning circuits at high rates and result in generalized improvements in sensory perception offer appealing therapeutic options for perceptual disorders that have traditionally been considered untreatable (23, 24), making the study of sensory-guided foraging behavior both theoretically interesting and clinically relevant.

Much like our foraging ancestors, the modern urbanite faces the challenge of guiding his/her behaviors using noisy, dynamic sensory cues. Examples of these conditions abound in the auditory domain, where distractors can impede communication with friends at social gatherings, instruction from teachers in classrooms, or transmission of information via a cellular phone. As the extraction of weak signals from background distractors represents a universal perceptual problem, presenting in the hearing impaired and typically hearing alike (25–30), it offers a good test case for the malleability of perceptual skill following practice on an auditory foraging task.

Using a combination of psychophysical measurements and in vivo neurophysiological recordings in humans and mice, respectively, we examined (*i*) whether subjects could improve their efficiency on a closed-loop auditory foraging task requiring them

Significance

All sensory systems face two fundamental limitations: (*i*) segregating partially overlapping sensory inputs into separate perceptual objects and (*ii*) raising sensory events that are either weak or noisy to perceptual awareness. The ability of sensory systems to extract information from weak signals in noisy backgrounds can improve with practice, but learning does not typically generalize to untrained stimuli. By training humans and mice with an audio game inspired by sensory foraging behavior, we show that learning to discriminate simple, easily controlled sounds can generalize to improved neural and perceptual processing of “real-world” complex sounds, including speech in noise. These findings suggest new therapeutic options for clinical populations that receive little benefit from conventional sensory rehabilitation strategies.

Author contributions: J.P.W., K.E.H., and D.B.P. designed research; J.P.W. and D.B.P. performed research; K.E.H. contributed new reagents/analytic tools; J.P.W. analyzed data; and J.P.W. and D.B.P. wrote the paper.

The authors declare no conflict of interest.

This article is a PNAS Direct Submission.

¹To whom correspondence may be addressed. E-mail: jpwit05@mit.edu or daniel_polley@mei.harvard.edu.

This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1322184111/-DCSupplemental.

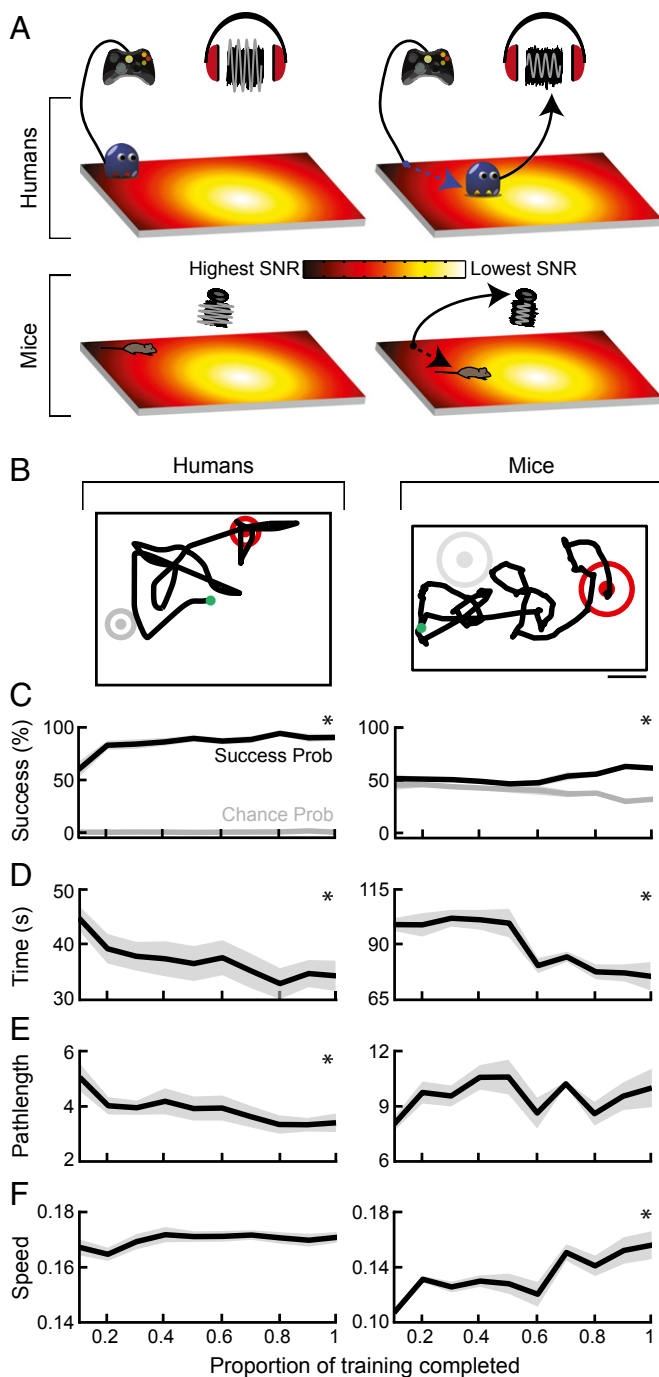


Fig. 1. Humans and mice learn to use dynamic auditory cues to locate hidden targets. (A, Upper) Humans played an audio game wherein the movements of an avatar were controlled with a game pad, while (Lower) mice trained in a physical behavioral arena. The heat map corresponds to SNR. (B) A representative trial for a human and a mouse illustrates casting and zigzagging behaviors along the sound gradient. The filled and open circles indicate the center and perimeter of the target (red) and "dummy" (gray) zones. The green dots indicate position at the start of the trial. (Scale bar: 10 and ~ 3.5 cm for the mouse and human arena, respectively.) Time spent in "dummy" targets provides the basis for calculating target identification by chance alone. (C) Percentage of trials in which humans (Left) and mice (Right) located the target within the time constraints across the training period. (D) Time and (E) length of path required to complete trial as a function of training time. Path length taken to reach the target was normalized by the diagonal distance of the training arena. (F) Likewise, running speed is reported as normalized distance per second and plotted as a function of training time. The line plots reflect mean \pm SEM. Significant learning effects are indicated with an asterisk in the upper right-hand corner of the plot.

to continuously discriminate changes in the level of a faint sound embedded in masking noise, (ii) the behavioral strategies used to solve the foraging task, (iii) if, in humans, learning in the context of foraging transferred to untrained tests of speech recognition in the presence of distractors, and (iv) if, in mice, foraging experience altered the neural representation of target signals and distractors in primary sensory cortex. We found that, although both humans and mice learned to improve their foraging efficiency with practice, disparate behavioral strategies were used both within and across species. Furthermore, behavioral improvements on the foraging game were associated with improved speech perception in noise abilities in humans and enhanced neural representation of weak, noisy signals in primary auditory cortex of mice.

Results

Humans and Mice Learn to Forage in a Soundscape for Hidden Rewards. Human participants played an auditory foraging game for approximately one-half hour per day (33 ± 1 min) over the course of 1 mo. The objective of the game was to use a remote-controlled avatar to search a 2D, virtual soundscape for the location of a hidden target before time expired (Fig. 1A, Upper). The target location varied randomly from trial to trial. Visual search cues were not provided. The only available cue to locate the hidden target came from the level of a 500-Hz tone presented in a constant level of broadband masking noise. To make the task perceptually demanding, the level of the tone relative to distractor [signal-to-noise ratio (SNR)] was decreased in real time according to the Euclidean distance between the subject and the hidden target location (Fig. 1A). Mice were engaged in a live-action version of the game played by humans, wherein they also foraged within a 2D soundscape to find the location of a low SNR target and receive a water reward (Fig. 1A, Lower). Thus, mice and humans learned to develop adaptive movement strategies that would reveal subtle changes in SNR, allowing them to find the virtual target location and receive reward.

Consistent with observations in insects (4) and mammals (5, 31) (including humans) moving along odor gradients, we rarely observed direct paths to the target location. Rather, we typically noted sweeping initial searches that were ultimately refined as the subjects closed on the target location. On some trials, these paths resembled the casting and zigzagging search strategies used by insects operating on sporadic cues and partial information (4) (Fig. 1B). Over the course of training (humans, 1 mo; mice, 3 mo), both species learned to find the auditory target location more successfully ($n = 10$ humans, $P = 5 \times 10^{-7}$; $n = 4$ mice, $P = 2.9 \times 10^{-3}$, Friedman test; Fig. 1C) and to identify the target location more quickly (humans, $P = 3 \times 10^{-5}$; mice, $P = 3 \times 10^{-3}$, Friedman test; Fig. 1D). For humans, but not mice, the reduced time to target was accompanied by a decrease in average travel distance per trial (humans, $P = 3 \times 10^{-4}$; mice, $P = 0.13$, Friedman test; Fig. 1E). By contrast, in mice, but not humans, search speed progressively increased over training (humans, $P = 0.34$; mice, $P = 6 \times 10^{-4}$, Friedman test; Fig. 1F). This double dissociation between adaptive changes in path length and speed led us to hypothesize that the humans and mice solved the foraging task differently.

Humans and Mice Use Different Strategies to Solve the Auditory Foraging Task. To delineate the strategies used by humans and mice in this task, we analyzed their moment-by-moment behavioral decisions by dividing behavioral traces from training trials (Fig. 2A–C, Far Left in black) into movement vectors that were sampled every 0.3 s (Fig. 2A–C, colored arrows). At any given time point, the optimal bearing toward the target could be calculated between the forager's current position and the target location (Fig. 2D). By subtracting the forager's movement vector at each 0.3-s behavioral "moment" from the ideal bearing, we

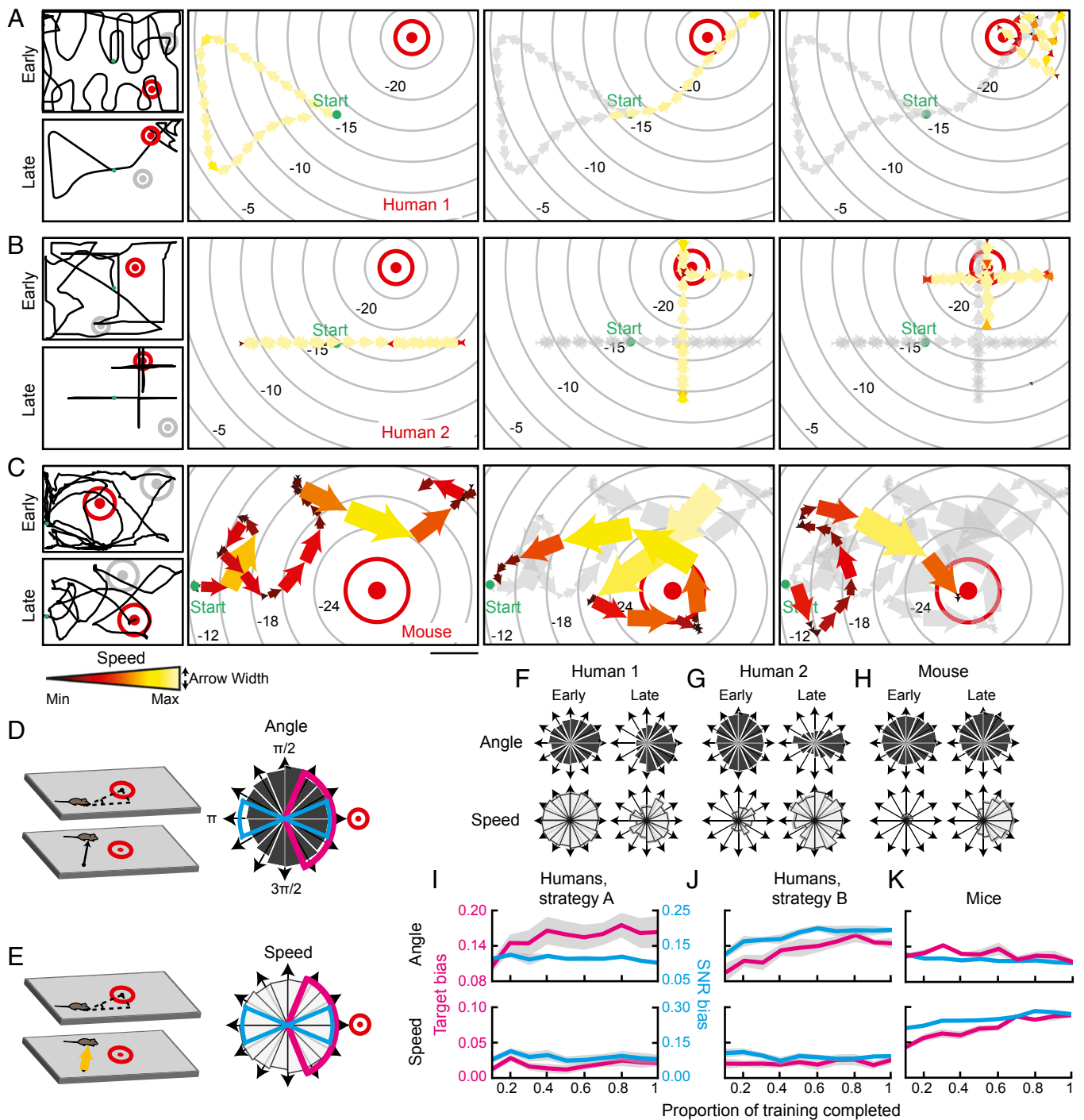


Fig. 2. Adaptive sensory-guided foraging strategies emerge with practice. (*A–C, Far Left*) Individual early and late training trials for two humans and a mouse. (*Right*) Movement speed and trajectory from sequential epochs of the corresponding “late” exemplar trial (time progresses from left to right). The concentric circles demarcate the mapping of auditory SNR onto the 2D training arena. Direction of arrowheads reflect trajectory, color of arrows represents search speed normalized at the trial level, and arrow size reflects search speed normalized across all three examples. The gray arrows are superimposed from the previous time epoch(s). (Scale bar: 10 and ~3.5 cm for the mouse and human arena, respectively.) The filled and open circles indicate the center and perimeter of the target (red) and “dummy” (gray) zones. The green dots indicate position at the start of the trial. (*D*) The difference between actual trajectory and the ideal bearing is calculated every 0.3 s. Adaptive search strategies could emphasize movements toward the target (target bias, magenta) or along the steepest slope of the SNR gradient (SNR bias, cyan). (*E*) Like angular target and SNR bias, normalized search speed can also be expressed across movement trajectories. (*F–H*) Normalized distributions of (*Upper*) search trajectories and (*Lower*) speed modulation early vs. late in training for the two example human subjects (*F* and *G*) and one mouse (*H*). [Speed axis bar: 0.13–0.19 d/s in humans and 0.09–0.21 d/s in the mouse; mean speed (white foreground); SEM (gray background).] (*I–K*) Target and SNR bias in movement trajectories (*Upper*) or speed (*Lower*) for human subjects who used foraging strategy A (*I*; $n = 4$) or B (*J*; $n = 6$), and all trained mice (*K*; $n = 4$) plotted as a function of training time. Foraging strategy A is defined by an exclusive increase in toward target bias with training (four subjects, including Human 1, used this strategy), while foraging strategy B is defined by increased SNR and toward target bias (six subjects, including Human 2, used this strategy). The line plots reflect mean \pm SEM.

were able to represent, with search trajectories, how the forager's movements deviated from the optimal trajectory. For both species, we found that search trajectories were fairly randomly distributed early in training (Fig. 2 *F–H*, Upper). By later stages in training, we found that search trajectories in humans were generally biased toward the target (Fig. 2*F*) and, in many cases, along the most informative SNR vector within the sound gradient (i.e., greatest increase or decrease in tone amplitude per unit distance; Fig. 2*G*). We quantified target bias as the degree to which subjects moved along any angle that took them closer to the target (Fig. 2*D*, magenta) and SNR bias as the degree to which subjects selected movement trajectories that provided the greatest SNR change per unit distance (either directly toward or away from the target; Fig. 2*D*, cyan). We found that all human foragers were more likely to increase their angular target bias over the course of training ($P = 2 \times 10^{-6}$, Friedman test; Fig. 2*I* and *J*, Upper, and Fig. S1). This class of search strategy typically began with high-speed, wide excursions and multiple turns to likely reveal the general flow of the gradient, followed by a winding, slower local search that was most often directed toward the target (Fig. 2*A*). In addition, 6 of 10 human subjects also developed an SNR bias over the course of training ($P = 5 \times 10^{-3}$, Friedman test; Fig. 2*J* and Fig. S1). These subjects essentially performed coordinate descent optimization by creating orthogonal excursions along the axes within the soundscape associated with the steepest slopes in the SNR gradient (Fig. 2*B* and *G*, Upper). Improved use of either strategy allowed human subjects to identify the hidden target with a reduced path length (Fig. 1*E*). As befitting their relatively constant path length over training, mice did not exhibit an improvement in target or SNR bias. If anything, their search trajectories became more random over the course of training (target bias, $P = 0.31$; reduction in SNR bias, $P = 0.02$, Friedman test; Fig. 2*H* and *K*, Upper, and Fig. S1).

Their improved success in the foraging task (Fig. 1*C*) and overall increase in running speed (Fig. 1*F*) suggested that mice used an alternate gradient-based strategy to solve the foraging task. When navigating a light gradient, *Chlamydomonas nivalis*, a species of green algae, has been observed to be directly photokinetic, modulating its speed in a graded fashion relative to the "ideal" angle toward a light source (32). We tested whether mice might use a similar gradient-based strategy by calculating the running speed of each mouse with respect to the angular deviation from the optimal bearing (Fig. 2*E*). At early stages of training, running speed was not modulated by the mouse's chosen angle. However, over the course of training, mice learned to increase their running speed when moving toward the target and along bearings associated with the most pronounced SNR changes (target bias, $P = 3 \times 10^{-4}$; SNR bias, $P = 5 \times 10^{-4}$, Friedman test; Fig. 2*C*, *H*, Lower, and *K*, Lower, as well as Fig. S1). Humans were not observed to modulate their running speed by either strategy (target bias, $P = 0.79$; SNR bias, $P = 0.42$, Friedman test; Fig. 2*I* and *J*). These findings suggested that humans and mice used different types of adaptive foraging strategies; humans learned to bias their search trajectories toward the target and in most cases also along the steepest slopes in the SNR gradient, whereas mice continued to move along a variety of angles but selectively increased their running speed according to real-time changes in SNR.

Foraging Strategies Depend on Local Sensory Environment. As a final step, we asked how foraging strategies learned over a period of weeks were dynamically coordinated over the course of a single trial. We first characterized whether target and SNR angular biases observed in human foragers depended on sensory context by measuring each type of bias according to position within the overall SNR gradient (Fig. 3*A* and *B* and Fig. S2). Well-trained human subjects exhibited target bias at all SNRs (Fig. 3*A*, Up-

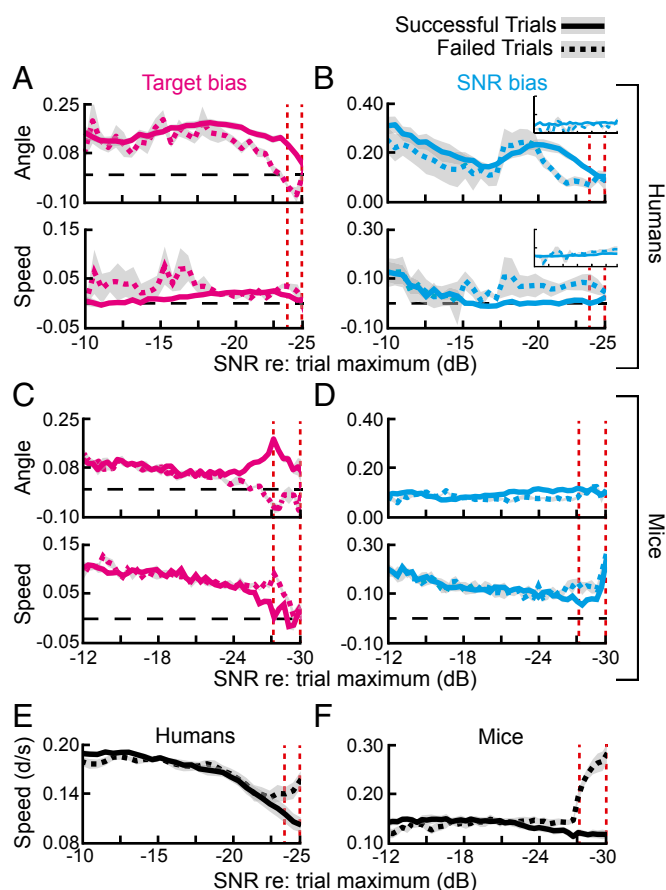


Fig. 3. Foraging strategy is modulated by local sensory context. This visualization breaks down the overall foraging biases plotted in Fig. 2 according to spatial position within the SNR training arena. For all plots, behavioral data are shown from well-trained subjects (second half of training) according to spatial proximity to the target, expressed as SNR. The broken vertical red lines indicate target SNRs. The solid and broken lines reflect data from successful (i.e., rewarded) and failed trials, respectively. The broken horizontal black bars indicate unbiased foraging behavior. (A and C) Target bias in angular search trajectory (Upper) and speed (Lower) for all humans (A) and mice (C). (B and D) SNR bias in angular search trajectory (Upper) and speed (Lower) for humans (B) and mice (D). SNR bias is plotted separately for subjects using strategy B vs. those that did not (strategy A, Inset). (E and F) Overall search speed is plotted as a function of distance from target in humans (E) and mice (F). The unit of measurement for speed (d/s) is distance traveled, normalized to the diagonal length of the training arena, per second. Data are plotted as mean \pm SEM.

per). Human subjects who performed coordinate descent optimization in the soundscape (strategy B) demonstrated SNR bias in their search trajectories at low and high SNRs. There was a dip in SNR bias at moderate SNRs that roughly coincided with the peak of the angular target bias function, suggesting that foragers who used gradient descent strategies may have flexibly switched between gradient orientation at the lowest and highest SNRs and target bias at intermediate SNRs (SNR effect, $P = 9.1 \times 10^{-11}$, ANOVA; Fig. 3*A* and *B*, Upper). Contrasting trials in which subjects successfully located the target within the allotted time (solid lines) vs. those where they did not (dashed lines), revealed that failures in successful foraging were distinguished by strategic search differences within a region close to the low SNR target (enclosed by vertical, red lines, Target Bias, Correct vs. Failed by SNR interaction, $P = 4.3 \times 10^{-6}$; SNR bias, Correct vs. Failed by SNR interaction, $P = 0.69$, ANOVA; Fig. 3*A* and *B*, Upper).

Although our trial-level analysis suggested that mice did not use angular target bias as a search strategy in the foraging task, our more detailed SNR-based analysis revealed that mice did, in fact, use this strategy, albeit only at low SNRs that were local to the target ($n = 4$, SNR effect, $P < 3 \times 10^{-16}$, ANOVA; Fig. 3C, Upper). At higher SNRs, we found that mouse running speed was modulated with a combination of angular target and SNR bias (Speed Target Bias; SNR effect, $P < 3 \times 10^{-16}$, Speed SNR bias; SNR effect, $P < 3 \times 10^{-16}$, ANOVA; Fig. 3C and D, Lower). Similar to the human subjects, we noted that failures in foraging success for mice were associated with strategic differences restricted to a low SNR region local to the target (Target Bias, Correct vs. Failed by SNR interaction, $P < 3 \times 10^{-16}$; Speed Target Bias, Correct vs. Failed by SNR interaction, $P = 1.2 \times 10^{-10}$; Speed SNR bias, Correct vs. Failed by SNR interaction, $P = 0.03$, ANOVA).

Finally, to further examine the dependence of foraging strategy on sensory cues, we analyzed the overall search speed as a function of SNR (Fig. 3E and F). Across both species, we found that search speed decreased at the lowest SNRs on successful trials (humans, SNR effect, $P < 3 \times 10^{-16}$; mice, SNR effect, $P < 3 \times 10^{-16}$, ANOVA; Fig. 3E and F). Importantly, unsuccessful trials were characterized by a failure to modulate search speed with sensory cues for these same SNRs (humans, Correct vs. Failed by SNR interaction, $P = 0.04$; mice, Correct vs. Failed by SNR interaction, $P < 3 \times 10^{-16}$, ANOVA; Fig. 3E and F).

To summarize, across both species, we observed that at favorable SNRs, a high speed search was conducted, driven by

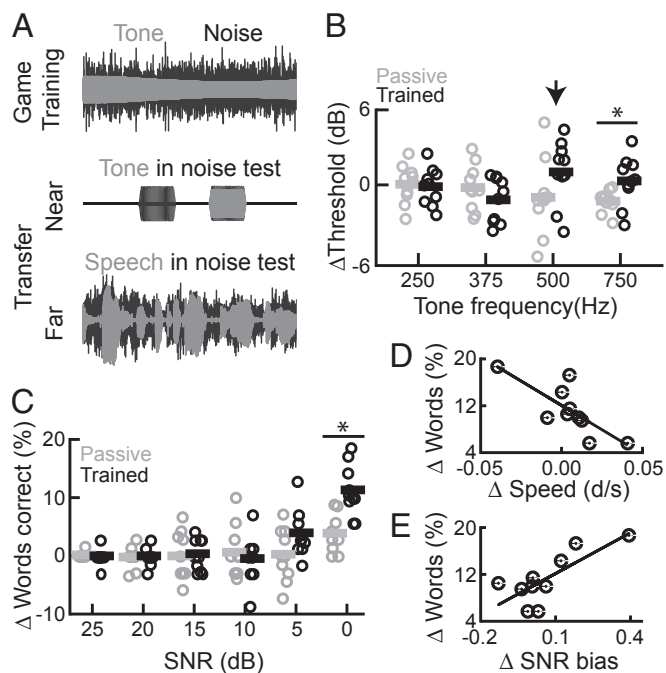


Fig. 4. Learned improvements in auditory-guided foraging generalize to distinct listening tasks. (A) The physical stimulus waveform used in the foraging task (Top) is similar to the stimulus used for the tone in noise task (Middle) but dissimilar to the test of speech perception in multitalker babble (Bottom). (B) Change in tone detection thresholds (Post – Pre) assessed at four tone frequencies (training frequency indicated by arrow). (C) Change in words correctly recognized for the speech in noise task (Post – Pre) plotted according to target speaker SNR. (D and E) Correlation between change in search speed (D) and SNR bias (E) at locations between 0 and 5 dB SNR and improved performance on the speech in noise test at 0 dB SNR. The horizontal lines in scatter plots reflect group means. The asterisks indicate statistically significant differences between groups.

either choosing search trajectories that were biased toward the target and steepest changes in the SNR gradient (humans) or modulating running speed with angular target and SNR bias (mice). As the foragers moved to lower SNRs (local to the target), slower, systematic exploration dominated the search strategy, representing a strategy switch from speed modulation to choosing more accurate search trajectories in mice. Across all foragers, the behavioral strategies used to successfully solve the foraging task were only disrupted at the lowest SNRs on failed trials, suggesting that failures in slow, systematic, local exploration at locations providing the most degraded sensory feedback accounted for limitations in trial-level success.

Learning on the Auditory Foraging Task Transfers to an Untrained Speech Perception Task.

We next asked whether increased proficiency in the auditory foraging game generalized to other measures of auditory perception. Psychophysical tests were performed on human subjects who had been randomly assigned either to train on the foraging game for 1 mo or had been passively exposed to game stimuli for the same time period (Fig. 4A). First, we assessed near transfer (Fig. 4A, Middle) by measuring detection thresholds for pure tones (250, 375, 500, and 750 Hz) presented in the presence of a simple broadband masker before and after foraging or passive listening. We observed increases in response thresholds for trained subjects compared with passively exposed controls that were specific to the frequency channels (based on peripheral excitation patterns) used in the foraging task (Group by Test frequency interaction, $P = 0.05$; 250 Hz, $P = 1.38$; 375 Hz, $P = 0.24$; 500 Hz, $P = 0.17$; and 750 Hz, $P = 0.04$, ANOVA followed by post hoc two-sample t tests with Holm–Bonferroni correction for multiple comparisons; Fig. 4B). This finding of stimulus-specific elevated detection thresholds following a task that relied primarily on stimulus discriminations is consistent with previous observations (33, 34).

We next tested whether observed improvements in using weak tones in noise to guide behavior in the auditory foraging task also transferred to more ethologically relevant situations such as understanding speech in noisy environments (Fig. 4A and C, and Fig. S3A–C). Toward this goal, we administered the Quick Sentence in Noise Test, a common clinical tool used to assess real-world speech in noise perception. We found that subjects who trained on the foraging task improved their word recognition scores at the most difficult SNR tested (0 dB SNR) by an average of 12% (Fig. 4C). This represented a significant improvement compared with the passive exposure group (Group by SNR interaction, $P = 8 \times 10^{-4}$; 0 dB SNR, $P = 1 \times 10^{-3}$, ANOVA followed by post hoc two-sample t tests with Holm–Bonferroni correction for multiple comparisons; Fig. 4C and Fig. S3A and B) with large effect sizes measured at both +5 and 0 dB SNR (effect sizes, 0.8 and 1.9, respectively; Hedges' g). The small speech in noise improvements demonstrated by the passively exposed group are expected based on learning that occurs during the pretest evaluation (35). Combined with the stimulus-specific modulation of tone detection thresholds reported above, these far transfer findings demonstrate that training on an auditory foraging task is associated with both stimulus-specific and generalized learning effects.

We then examined whether improved comprehension of the most degraded speech in noise samples could be predicted from individual differences in game play strategy. Although more traditional measures such as success rate or time to target were not significantly predictive of learning transfer (Fig. S4), we found that dynamic search behaviors, specifically in low SNR conditions close to the target, were significantly predictive of improved processing of highly degraded speech (0 dB SNR; Fig. 4D and E). Specifically, subjects who learned to slow their search speeds and to move along the steepest slope of the SNR gradient when within 5 dB of the target demonstrated the

Improved Foraging Ability Is Associated with a Reorganized Cortical Representation of Weak Tones. We examined the neural correlates of learning on the auditory foraging task by making unit recordings from the auditory cortex (A1) of mice that were trained on the task or passively exposed to the same auditory stimuli but did not participate in the task. We hypothesized that training on the task would be associated with an altered representation of trained stimulus features, such that the representational salience of weak, noisy inputs would be enhanced. We first collected frequency response areas (FRAs) in both groups of mice by presenting pure tones with pseudorandomly varied frequencies between 4 and 48 kHz and intensity levels from 0 to 80 dB sound pressure level (SPL) (Fig. 5A). Training was associated with a marked overrepresentation of characteristic frequencies (CFs) (the preferred frequency at threshold) near the 16-kHz training frequency compared with passively exposed controls ($n = 151$ neural recording sites from four trained mice; $n = 180$ neural recording sites from four passively exposed mice; $P = 6 \times 10^{-4}$, two-sample Kolmogorov–Smirnov test; Fig. 5B). This proportional increase in frequency tuning was not limited to 16 kHz, but rather extended a half octave above and below the training frequency. Because the foraging task emphasized recognition of subtle variations in tone level, we examined the encoding of sound frequency across the full range of levels encountered in the task.

In passively exposed control mice, increasing the tone level above threshold was associated with a monotonic increase in firing rate and little change in best frequency, as has previously been described in rodent A1 (38) (Fig. 5A, C, and D). In trained mice, we observed that many rate-level functions were nonmonotonic, decreasing their firing rate in response to high-level stimuli ($P = 9 \times 10^{-13}$, two-sample t test; Fig. 5C and D) and, accordingly, were often best driven by relatively faint tone levels, near the target intensity range in the foraging task ($P = 3 \times 10^{-10}$, two-sample Kolmogorov–Smirnov test; Fig. 5E). By contrast to units recorded in passively exposed controls, many FRAs recorded in trained mice “leaned,” such that best frequency shifted downward by nearly one octave across the range of sound levels tested here (Group effect, $P < 3 \times 10^{-16}$; Level effect, $P < 3 \times 10^{-16}$; Group by Level interaction, $P < 3 \times 10^{-16}$, ANOVA; Fig. 5A and F). Finally, we plotted the mean normalized neural response across all recording sites to characterize how the combination of the described distortion in frequency tuning, increase in nonmonotonicity in level tuning, and the interaction of frequency tuning with presentation level might alter the representation of sounds in the absolute frequency/intensity coordinates. We found that, in the trained animals, population neural activity maximized responsiveness across the frequency–intensity range of the target (Fig. 5G and H).

Neural Responses in Trained Animals Are Resistant to Suppression by Continuous Background Noise. The SNR foraging task places a premium on suppressing the distraction imposed by the masking noise as well as enhancing the representational salience of low-level tones at the target frequency. To better understand how A1 responses were modified according to both of these perceptual demands, we derived tonal receptive fields under a background of continuous broadband masking noise ranging from 40 to 70 dB SPL. In passively exposed mice, increasing masker amplitude suppressed tone-evoked spiking, elevated thresholds, and restricted the range of frequency tuning (Fig. 6A and Fig. S5). However, FRAs measured in trained mice were more resistant to noise degradation at levels matching the background distractor intensities encountered in the foraging task (40–50 dB SPL; Fig. 6A and Fig. S5). We next asked whether this reduced suppression of neural responses to tones in the presence of a continuous distractor might also result in an improved neural SNR. Thus, at each recording site, we calculated the ratio between the response

to the target signal (low level, 16-kHz tones) and the response to the continuous distractor. We found that the neural SNR index was significantly higher in the trained than passively exposed animals in the quiet condition and in the presence of low (40–50 dB SPL) but not high (60–70 dB SPL) noise levels (Group effect, $P = 0.18$; Noise effect, $P < 3 \times 10^{-16}$; Group by Noise level interaction, $P = 1 \times 10^{-4}$; Quiet, $P = 3 \times 10^{-3}$; Low Noise, $P = 9 \times 10^{-4}$; High Noise, $P = 0.02$, ANOVA followed by post hoc two-sample t tests with Holm–Bonferroni correction for multiple comparisons; Fig. 6B). Further analysis revealed that this improvement in neural SNR was largely due to a decrease of the neural response to the ongoing white-noise stimulus across noise levels, whereas the response to target signals were equivalent between the groups (Noise Response, Group effect, $P = 2 \times 10^{-5}$; Noise level effect, $P = 0.12$; Group by Noise level interaction, $P = 0.30$; Signal Response, Group effect, $P = 0.1$; Noise level effect, $P < 3 \times 10^{-16}$; Group by Noise level interaction, $P = 0.32$; Fig. 6C).

SNR Foraging Enhances the Neural Coding of Weak Signals. As a final step to characterize changes in the cortical representation of task-relevant acoustic parameters, we analyzed rate-level functions at the training frequency under varying levels of background noise. In passively exposed mice, the steeply sloping region of the rate-level functions shifted according to the masking noise level. Under levels of masking noise encountered in the training task (50 dB), this shift reduced the availability of dynamic firing rate cues for tone levels associated with the target (Fig. 6D and Fig. S6). By contrast, in trained mice, we found that the steepest slopes of the firing rate functions remained inside the range of weak signal levels that served as targets in the foraging task regardless of the masker level (Fig. 6D and Fig. S6). This relationship is captured by the first derivative of the rate-level function, which confirmed significantly steeper growth of response across weak signal levels in trained mice compared with passively exposed controls (Group effect, $P = 1 \times 10^{-3}$; SNR effect, $P = 3 \times 10^{-16}$; Group by SNR interaction, $P = 0.3 \times 10^{-16}$; –15–0 dB SNR, $P < 3 \times 10^{-6}$, ANOVA followed by post hoc two-sample t tests with Holm–Bonferroni correction for multiple comparisons; Fig. 6E, Upper, and Fig. S7). Often, the steeply sloping region of a growth function contains the most information for coding differences between stimuli because the contrast between neural responses to similar physical stimuli is high and the variability in trial-by-trial responses is low. This can be expressed quantitatively using Fisher information (39) for neural responses obtained from trained and passively exposed mice. Under low-noise conditions, Fisher information was low for weak signals in passively exposed mice, reaching a maximum at levels just above the masker. By contrast, the Fisher information function peaked at weak signal levels in the trained mice, perhaps supporting the perceptual demands of the auditory foraging task (Fig. 6E, Lower, and Fig. S7).

To test whether task-related plasticity conferred any adaptive benefit to sound coding, we used an *in silico* poststimulus time histogram (PSTH)-based classifier (40) to decode tone stimulus intensity across the populations of neurons recorded in trained or passively exposed mice. In this template matching model, the neural response is classified as belonging to the stimulus class to which its Euclidean distance is shortest. We found that the classification of sound level using the neural data from the trained animals was superior to that of the passive controls under low-noise conditions, indicating that the representational plasticity in trained animals supported an improved neural code for stimulus properties encountered in the foraging task (Quiet, $P = 0.12$; Low Noise, $P = 6 \times 10^{-3}$; High Noise, $P = 0.14$, bootstrapped permutation test for difference in means with Holm–Bonferroni correction for multiple comparisons; Fig. 6F).

Discussion

By tapping into an evolutionarily conserved behavior, we were able to compare learning on a closed-loop audiomotor task in two commonly used species for neuroscience research. We expected that movement trajectories would coalesce around the general direction of the target as subjects learned to use sensory cues to guide foraging behavior. Although this “target bias” in foraging strategy was used to some degree by all human subjects over the course of training, we also found that some subjects also learned to restrict their search trajectories to the steepest, most informative slope in the SNR gradient (both toward and away from the target). A similar strategy has been described in the echolocating Egyptian fruit bat when “locking” to a target and has been computationally shown to provide optimal discriminatory feedback for localization at the expense of detection (41). Employment of an SNR bias strategy suggests that, as sensory information accumulated, most humans built a detailed model of the sensory search space. Evidence of similar modeling of the search space was not generally observed in mice. We found that mice increased angular target bias only at low SNRs, during slow search on the foraging task. By contrast to humans, most of their foraging efficiency improvements were attributable to an increased running speed when moving toward the target, a phenomenon that has previously been observed in green algae during phototaxis (32).

Following 1 mo of training on an auditory foraging task with simple acoustic stimuli, we observed significant transfer of learning to an untrained task of speech recognition in the presence of four-talker babble that was well predicted by game performance. Learning transfer to a more complex signal in noise task was surprising given that stimulus specificity has been repeatedly associated with sensory learning since the seminal report of Fiorentini and Berardi (42) over 3 decades ago. However, recent studies have cast doubt on the inviolate specificity of perceptual learning, suggesting that the particular training methodology may influence the degree of learning transfer (43–48). For example, experience with action video games has been associated with accelerated learning of non-native phonetic contrasts (49) and enhanced visual abilities on tasks ranging from useful field of view to contrast sensitivity (20, 21, 23, 24). The key elements of action video game play that lead to appreciable transfer of visual learning are not yet clearly understood. However, the varied perceptual demands in these tasks are congruent with many of the conditions that promote learning transfer on traditional perceptual learning paradigms (45–47, 50). Musicianship represents yet another form of sensorimotor learning that shares a number of qualities with the auditory foraging game (e.g., audiomotor feedback that is both immediate and directional) and has recently been associated with generalized enhancement of auditory skills (18, 19, 51). Interestingly, musicians have been shown to outperform nonmusicians on the same speech in noise perception test administered in the present study, with years of experience positively correlating with better performance (ref. 18; but see ref. 52). Thus, it is plausible that, due to the dynamic nature of the discriminanda, which, like roving reference paradigms, offers no “standard” reference stimulus, or because of the immersive game-based sensorimotor approach, learning in this auditory foraging task transferred to challenging listening contexts that were dissimilar, both acoustically and cognitively, from the conditions of the training task.

Another possible explanation for the observed learning transfer is that training to extract signals from noise might represent a more generalizable skill than the fine feature discrimination that is typically trained in perceptual learning studies. Evidence for this notion comes from a recent study in the visual system, which found that human participants who were trained to discriminate the orientation, motion, or displacement of random

dot stereograms in the presence of visual distractor noise, demonstrated learning transfer to both untrained stimulus dimensions (53). Although distractor stimuli in that study were similar across training and transfer test conditions, our results indicate that transfer effects can also be observed when both the stimulus and distractor in the transfer tests are more complex than the training stimuli (speech and four-talker speech babble vs. a pure-tone and broadband continuous noise). By systematically varying the spectrotemporal and linguistic structure of untrained targets and maskers in future studies, it may be possible to further elucidate the limits of far transfer effects (52).

Perceptual improvements conferred by both traditional learning paradigms and action video game play are thought to arise from reductions of internal noise and filtering of external noise (54, 55), increased efficiency (24, 56), and improved probabilistic inference (57–59). Pertinent to the experiments reported here, probabilistic inference was measured using a tone in noise lateralization task in the experiments reported by Green et al. (57), demonstrating some cross-modal transfer of learning to auditory signal in noise perception following video game play. In many of these studies, neural plasticity associated with training, expressed either as induced bias or increased connection strength, was localized to connections between higher cortical areas that update movement representations based on dynamic sensory information (54, 55, 57).

We explored the neural correlates of training in A1, a comparatively early stage of cortical processing where unit responses are known to be strongly modulated by auditory associative learning (10, 11, 60–65). We noted that neural responses of trained mice were globally suppressed relative to passive controls. However, response suppression was far more robust for tone frequencies far from the target or for broadband continuous maskers (Fig. 6C), resulting in a relative enhancement of target signal representation. Differential suppression of neural activity in primary auditory cortex has also been observed in ferrets during engagement in a signal in noise detection task (66), with suppression scaling indirectly with SNR and directly with performance. Similar findings have been reported in early auditory (62, 67, 68), visual (69, 70), and somatosensory cortices (71) of primates trained to discriminate targets from distractors. Although the training studies mentioned here, as well as the currently reported experiment, suggest that learning to extract signals from noise alters the relative neural representation of task-specific targets and distractors in primary auditory cortex (perhaps explaining behavioral improvements on trained tasks and stimulus-specific changes in tone-detection thresholds), the transfer effects observed in our study as well as another (53) suggest an additional stimulus-general effect of training, perhaps via response plasticity in sensory-motor brain areas (72, 73) or frontoparietal networks involved in sensory distractor suppression (22, 74–76). The latter possibility could be tested across species by making preforaging and postforaging training unit recordings in the primary auditory cortex of awake, behaving mice and recording steady-state auditory evoked potentials in behaving humans to examine attentional modulation of target and distractor responses.

The ability to improve generalized, auditory signal in noise perception through a learning paradigm makes it an appealing therapeutic for certain clinical populations. There are an estimated 48 million individuals living with hearing impairment in the United States alone (77). Even after treatment with hearing aids or cochlear implants, these individuals present with substantial deficits when attempting to extract target speech signals from background talkers. There are several potential factors that contribute to this difficulty, some of which are associated with peripheral pathology [e.g., reduced spectral resolution of auditory filters (78)], and others with impaired central processing (79–81). As the need to quickly and reliably extract signals from background noise is ubiquitous in

work, educational, and social contexts, improved signal in noise extraction in these listening environments may improve quality of life for these individuals.

Materials and Methods

Auditory Foraging Task Procedures. All procedures performed with humans were approved by the Human Studies Committees at Massachusetts Eye and Ear Infirmary and the Massachusetts Institute of Technology. Twenty young adult subjects with audiologically confirmed normal hearing sensitivity were randomly assigned to train on the auditory foraging task for 1 mo (30 min per day for 5 d per week) or to be passively exposed to the training stimuli over the same time period. Humans controlled the movements of an avatar in a 2D virtual arena using a game pad in the context of a custom audio game. The game was downloaded on the participants' laptop PCs and circumaural headphones were provided. Humans used audio feedback (level of a continuous 500-Hz tone) to guide their avatar to a location associated with the lowest sound level. A broadband masker of ~65 dB SPL (calibrated at their initial visit) was played continuously as a distractor. Like the mice, human subjects received no verbal instructions about the goals of the game; rather, they learned to forage for rewards (points) through trial and error.

All procedures performed with mice were approved by the Animal Care and Use Committee at Massachusetts Eye and Ear Infirmary and followed the guidelines established by the National Institutes of Health for the care and use of laboratory animals. Eight male CBA-CaJ mice, aged 6 wk, were water restricted and their light/dark cycles were reversed. Four mice were chosen to train on the auditory foraging task, and the other four served as passively exposed controls. Passive exposure was implemented through yoking; while one mouse was training, their yoked counterpart was placed in an elevated listening chamber situated inside the training arena. The auditory foraging task for mice was similar to the game played by humans except that it occurred in a physical (rather than virtual) space (40 × 65 cm, sound treated, training arena with overhead tweeter) and used a 16-kHz carrier frequency for the tone. The position of the mouse relative to the target was monitored with a webcam and custom software. If the mouse was able to navigate to the target location (a 14-cm-diameter circle) and remain within this space for 2 s, the auditory stimulus stopped, indicating that the mouse could return to the water spout for a reward of variable magnitude.

Auditory Foraging Task Data Analysis. For the moment-by-moment behavioral analysis, we divided behavioral traces from training trials into movement vectors that were subsampled every 0.3 s. At any given time point, the optimal bearing toward the target could be calculated between the forager's current position and the target location. By subtracting the forager's actual movement vector at each 0.3-s behavioral "moment" from the ideal bearing, we were able to represent, with search trajectories, how the forager's movements deviated from the optimal search vector. Toward target bias of search trajectories was quantified as the mean cosine of difference vectors across each trial (max possible value, 1). SNR bias was quantified in a similar fashion using the absolute value of the sine of the vectors subtracted from random performance, defined as the sine of an average vector angle of $\pi/4$ (maximum possible value, 0.707). Speed target bias and SNR bias were quantified in the same manner as described for the angular measures. The difference between these two methods was that the length of each behavioral response vector was defined as the speed at which the animal or avatar was moving (rather than 1). All vectors were binned into 1 of 16 categories from

0 to $15\pi/8$ rad in increments of $\pi/8$. The mean speed was calculated for all response vector categories and then normalized before the cosine or sine of the vectors was determined.

Tests of Learning Transfer. All testing was performed in a sound-treated research booth. We tested whether learning on the foraging task transferred outside of the task demands by making preintervention and postintervention measurements of signal in noise perception using both tonal and speech stimuli. Tone in noise detection thresholds were measured using a two-interval, two-alternative forced-choice procedure. Stimuli were generated and the testing protocol was implemented using the *SoundGen* system (82) to adaptively identify the threshold for 79% response accuracy (83). Thresholds were measured for tones with carrier frequencies of 250, 375, 500, and 750 Hz. Speech perception in noise was measured using a standard clinical assessment tool called the Quick Sentence in Noise Test (84) that is meant to assess real-world hearing in noise abilities. This test requires that a listener extract and repeat a sentence (with low predictability) spoken by a target female speaker in the presence of four-talker babble at increasingly difficult SNRs.

Neurophysiological Recording Procedures. Trained ($n = 4$) and passively exposed ($n = 4$) mice were anesthetized, and a scalpel was used to make a 4 × 3 mm (rostrocaudal by mediolateral) craniotomy over the right auditory cortex. A 16-channel silicone probe (177- μm^2 contact area, 50- μm contacts on each of four shanks, 125 μm between shanks; NeuroNexus) was inserted orthogonal to the cortical surface to record multiunit responses from the middle cortical layers (0.3–0.5 mm).

All acoustic stimuli were delivered to the left ear of the mouse via custom miniature acoustic assemblies. FRAs were measured at each recording site by pseudorandomly presenting tone pips with carrier frequencies of 4–48.5 kHz in 0.12-oct steps at intensity levels from 0 to 80 dB SPL in 5-dB steps with and without continuous noise playing in the background.

Neurophysiological Data Analysis. The raw response traces were digitized and all subsequent analyses were performed in MATLAB (MathWorks) using custom scripts. Multiunit spikes were identified adaptively as voltage deflections that exceeded 4.5 SDs from the mean recorded activity. The boundaries of the FRAs (FRA mask) were defined objectively in most cases (85).

CF, Best level, and monotonicity were objectively defined using standard procedures. The index of neural signal-to-noise ratio was defined as $(S - N)/(S + N)$, where S is the average response (spikes per second) of each site to tones presented at 16 kHz (± 0.12 oct) and 35–60 dB SPL, and N represents the average spike rate at that site recorded over a 0.1-s window beginning 150 ms before stimulus onset. The first derivatives of smoothed rate level functions (5-point median filter) were approximated using a 5-point centered numerical algorithm. Fisher information functions were computed for each recording site using the methods described by Dean et al. (39). The PSTH classifier model was implemented using the approach described by Foffani and Moxon (40). Behavioral and neurophysiologic methods are further elaborated in *SI Materials and Methods*.

ACKNOWLEDGMENTS. We thank R. Williamson for computational assistance, D. Barbour for discussion, and R. Froemke for comments. Animal research was supported by National Institutes of Health Grants R01 DC009836 (to D.B.P.) and P30 DC5029. Human research was supported by a Mass Eye and Ear Curing Kids Award (to D.B.P.).

- Stephens D, Krebs J (1987) *Foraging Theory* (Princeton Univ Press, Princeton).
- Charnov EL (1976) Optimal foraging, the marginal value theorem. *Theor Popul Biol* 9(2):129–136.
- Greggers U, Menzel R (1993) Memory dynamics and foraging strategies of honeybees. *Behav Ecol Sociobiol* 32(1):17–29.
- Kennedy JS (1983) Zigzagging and casting as a programmed response to wind-borne odor—a review. *Physiol Entomol* 8(2):109–120.
- Porter J, et al. (2007) Mechanisms of scent-tracking in humans. *Nat Neurosci* 10(1):27–29.
- Thesen A, Steen JB, Døving KB (1993) Behaviour of dogs during olfactory tracking. *J Exp Biol* 180:247–251.
- Kolling N, Behrens TE, Mars RB, Rushworth MF (2012) Neural mechanisms of foraging. *Science* 336(6077):95–98.
- Hayden BY, Pearson JM, Platt ML (2011) Neuronal basis of sequential foraging decisions in a patchy environment. *Nat Neurosci* 14(7):933–939.
- Kvitsiani D, et al. (2013) Distinct behavioural and network correlates of two interneuron types in prefrontal cortex. *Nature* 498(7454):363–366.
- Bao S, Chang EF, Woods J, Merzenich MM (2004) Temporal plasticity in the primary auditory cortex induced by operant perceptual learning. *Nat Neurosci* 7(9):974–981.
- Polley DB, Heiser MA, Blake DT, Schreiner CE, Merzenich MM (2004) Associative learning shapes the neural code for stimulus magnitude in primary auditory cortex. *Proc Natl Acad Sci USA* 101(46):16351–16356.
- Bergan JF, Ro P, Ro D, Knudsen EI (2005) Hunting increases adaptive auditory map plasticity in adult barn owls. *J Neurosci* 25(42):9816–9820.
- Seitz A, Watanabe T (2005) A unified model for perceptual learning. *Trends Cogn Sci* 9(7):329–334.
- Parikh V, Kozak R, Martinez V, Sarter M (2007) Prefrontal acetylcholine release controls cue detection on multiple timescales. *Neuron* 56(1):141–154.
- Froemke RC, et al. (2013) Long-term modification of cortical synapses improves sensory perception. *Nat Neurosci* 16(1):79–88.
- Schultz W, Dayan P, Montague PR (1997) A neural substrate of prediction and reward. *Science* 275(5306):1593–1599.
- Leach ND, Nodal FR, Cordery PM, King AJ, Bajo VM (2013) Cortical cholinergic input is required for normal auditory perception and experience-dependent plasticity in adult ferrets. *J Neurosci* 33(15):6659–6671.
- Parbery-Clark A, Skoe E, Lam C, Kraus N (2009) Musician enhancement for speech-in-noise. *Ear Hear* 30(6):653–661.

19. Kraus N, Chandrasekaran B (2010) Music training for the development of auditory skills. *Nat Rev Neurosci* 11(8):599–605.
20. Green CS, Bavelier D (2003) Action video game modifies visual selective attention. *Nature* 423(6939):534–537.
21. Li R, Polat U, Makous W, Bavelier D (2009) Enhancing the contrast sensitivity function through action video game training. *Nat Neurosci* 12(5):549–551.
22. Anguera JA, et al. (2013) Video game training enhances cognitive control in older adults. *Nature* 501(7465):97–101.
23. Li J, et al. (2013) Dichoptic training enables the adult amblyopic brain to learn. *Curr Biol* 23(8):R308–R309.
24. Li RW, Ngo C, Nguyen J, Levi DM (2011) Video-game play induces plasticity in the visual system of adults with amblyopia. *PLoS Biol* 9(8):e1001135.
25. Sperling AJ, Lu ZL, Manis FR, Seidenberg MS (2005) Deficits in perceptual noise exclusion in developmental dyslexia. *Nat Neurosci* 8(7):862–863.
26. Ziegler JC, Pech-Georgel C, George F, Alario FX, Lorenzi C (2005) Deficits in speech perception predict language learning impairment. *Proc Natl Acad Sci USA* 102(39):14110–14115.
27. Kim SH, Frisina RD, Mapes FM, Hickman ED, Frisina DR (2006) Effect of age on binaural speech intelligibility in normal hearing adults. *Speech Commun* 48(6):591–597.
28. Ruggles D, Bharadwaj H, Shinn-Cunningham BG (2012) Why middle-aged listeners have trouble hearing in everyday settings. *Curr Biol* 22(15):1417–1422.
29. Kidd G, Jr., Arbogast TL, Mason CR, Walsh M (2002) Informational masking in listeners with sensorineural hearing loss. *J Assoc Res Otolaryngol* 3(2):107–119.
30. Marrone N, Mason CR, Kidd G, Jr. (2008) The effects of hearing loss and age on the benefit of spatial separation between multiple talkers in reverberant rooms. *J Acoust Soc Am* 124(5):3064–3075.
31. Khan AG, Sarangi M, Bhalla US (2012) Rats track odour trails accurately using a multi-layered strategy with near-optimal sampling. *Nat Commun* 3:703.
32. Hill NA, Hader DP (1997) A biased random walk model for the trajectories of swimming micro-organisms. *J Theor Biol* 186(4):503–526.
33. Sabin AT, Eddins DA, Wright BA (2012) Perceptual learning evidence for tuning to spectrotemporal modulation in the human auditory system. *J Neurosci* 32(19):6542–6549.
34. Fitzgerald MB, Wright BA (2005) A perceptual learning investigation of the pitch elicited by amplitude-modulated noise. *J Acoust Soc Am* 118(6):3794–3803.
35. Song JH, Skoe E, Banai K, Kraus N (2012) Training to improve hearing speech in noise: Biological mechanisms. *Cereb Cortex* 22(5):1180–1190.
36. Henderson Sabes J, Sweetow RW (2007) Variables predicting outcomes on listening and communication enhancement (LACE) training. *Int J Audiol* 46(7):374–383.
37. Olson AD, Preminger JE, Shinn JB (2013) The effect of LACE DVD training in new and experienced hearing aid users. *J Am Acad Audiol* 24(3):214–230.
38. Polley DB, Read HL, Storace DA, Merzenich MM (2007) Multiparametric auditory receptive field organization across five cortical fields in the albino rat. *J Neurophysiol* 97(5):3621–3638.
39. Dean I, Harper NS, McAlpine D (2005) Neural population coding of sound level adapts to stimulus statistics. *Nat Neurosci* 8(12):1684–1689.
40. Foffani G, Moxon KA (2004) PSTH-based classification of sensory stimuli using ensembles of single neurons. *J Neurosci Methods* 135(1–2):107–120.
41. Yovel Y, Falk B, Moss CF, Ulanovsky N (2010) Optimal localization by pointing off axis. *Science* 327(5966):701–704.
42. Fiorentini A, Berardi N (1980) Perceptual learning specific for orientation and spatial frequency. *Nature* 287(5777):43–44.
43. Jeter PE, Doshier BA, Liu SH, Lu ZL (2010) Specificity of perceptual learning increases with increased training. *Vision Res* 50(19):1928–1940.
44. Ahissar M, Hochstein S (1997) Task difficulty and the specificity of perceptual learning. *Nature* 387(6631):401–406.
45. Xiao LQ, et al. (2008) Complete transfer of perceptual learning across retinal locations enabled by double training. *Curr Biol* 18(24):1922–1926.
46. Harris H, Gilksberg M, Sagi D (2012) Generalized perceptual learning in the absence of sensory adaptation. *Curr Biol* 22(19):1813–1817.
47. Zhang JY, et al. (2010) Rule-based learning explains visual perceptual learning and its specificity and transfer. *J Neurosci* 30(37):12323–12328.
48. Resnik J, Sobel N, Paz R (2011) Auditory aversive learning increases discrimination thresholds. *Nat Neurosci* 14(6):791–796.
49. Lim SJ, Holt LL (2011) Learning foreign sounds in an alien world: Videogame training improves non-native speech categorization. *Cogn Sci* 35(7):1390–1405.
50. Green CS, Bavelier D (2012) Learning, attentional control, and action video games. *Curr Biol* 22(6):R197–R206.
51. Wong PCM, Skoe E, Russo NM, Dees T, Kraus N (2007) Musical experience shapes human brainstem encoding of linguistic pitch patterns. *Nat Neurosci* 10(4):420–422.
52. Ruggles DR, Freyman RL, Oxenham AJ (2014) Influence of musical training on understanding voiced and whispered speech in noise. *PLoS One* 9(1):e86980.
53. Chang DHF, Kourtzi Z, Welchman AE (2013) Mechanisms for extracting a signal from noise as revealed through the specificity and generality of task training. *J Neurosci* 33(27):10962–10971.
54. Doshier BA, Lu ZL (1998) Perceptual learning reflects external noise filtering and internal noise reduction through channel reweighting. *Proc Natl Acad Sci USA* 95(23):13988–13993.
55. Doshier BA, Lu ZL (1999) Mechanisms of perceptual learning. *Vision Res* 39(19):3197–3221.
56. Levi DM (2005) Perceptual learning in adults with amblyopia: A reevaluation of critical periods in human vision. *Dev Psychobiol* 46(3):222–232.
57. Green CS, Pouget A, Bavelier D (2010) Improved probabilistic inference as a general learning mechanism with action video games. *Curr Biol* 20(17):1573–1579.
58. Bavelier D, Green CS, Pouget A, Schrater P (2012) Brain plasticity through the life span: Learning to learn and action video games. *Annu Rev Neurosci* 35(35):391–416.
59. Bejjanki VR, Beck JM, Lu ZL, Pouget A (2011) Perceptual learning as improved probabilistic inference in early sensory areas. *Nat Neurosci* 14(5):642–648.
60. Recanzone GH, Schreiner CE, Merzenich MM (1993) Plasticity in the frequency representation of primary auditory cortex following discrimination training in adult owl monkeys. *J Neurosci* 13(1):87–103.
61. Polley DB, Steinberg EE, Merzenich MM (2006) Perceptual learning directs auditory cortical map reorganization through top-down influences. *J Neurosci* 26(18):4970–4982.
62. Blake DT, Heiser MA, Caywood M, Merzenich MM (2006) Experience-dependent adult cortical plasticity requires cognitive association between sensation and reward. *Neuron* 52(2):371–381.
63. Engineer CT, et al. (2014) Speech training alters tone frequency tuning in rat primary auditory cortex. *Behav Brain Res* 258:166–178.
64. Edeline JM, Pham P, Weinberger NM (1993) Rapid development of learning-induced receptive field plasticity in the auditory cortex. *Behav Neurosci* 107(4):539–551.
65. David SV, Fritz JB, Shamma SA (2012) Task reward structure shapes rapid receptive field plasticity in auditory cortex. *Proc Natl Acad Sci USA* 109(6):2144–2149.
66. Atiani S, Elhilali M, David SV, Fritz JB, Shamma SA (2009) Task difficulty and performance induce diverse adaptive patterns in gain and shape of primary auditory cortical receptive fields. *Neuron* 61(3):467–480.
67. Blake DT, Strata F, Churchland AK, Merzenich MM (2002) Neural correlates of instrumental learning in primary auditory cortex. *Proc Natl Acad Sci USA* 99(15):10114–10119.
68. Beitel RE, Schreiner CE, Cheung SW, Wang X, Merzenich MM (2003) Reward-dependent plasticity in the primary auditory cortex of adult monkeys trained to discriminate temporally modulated signals. *Proc Natl Acad Sci USA* 100(19):11070–11075.
69. Chen Y, et al. (2008) Task difficulty modulates the activity of specific neuronal populations in primary visual cortex. *Nat Neurosci* 11(8):974–982.
70. Boudreau CE, Williford TH, Maunsell JHR (2006) Effects of task difficulty and target likelihood in area V4 of macaque monkeys. *J Neurophysiol* 96(5):2377–2387.
71. Spingath EY, Kang HS, Plummer T, Blake DT (2011) Different neuroplasticity for task targets and distractors. *PLoS One* 6(1):e15342.
72. Znamenskiy P, Zador AM (2013) Corticostriatal neurons in auditory cortex drive decisions during auditory discrimination. *Nature* 497(7450):482–485.
73. Law CT, Gold JI (2008) Neural correlates of perceptual learning in a sensory-motor, but not a sensory, cortical area. *Nat Neurosci* 11(4):505–513.
74. Zanto TP, Rubens MT, Thangavel A, Gazzaley A (2011) Causal role of the prefrontal cortex in top-down modulation of visual processing and working memory. *Nat Neurosci* 14(5):656–661.
75. Bavelier D, Achtman RL, Mani M, Föcker J (2012) Neural bases of selective attention in action video game players. *Vision Res* 61:132–143.
76. Mishra J, Zinni M, Bavelier D, Hillyard SA (2011) Neural basis of superior performance of action videogame players in an attention-demanding task. *J Neurosci* 31(3):992–998.
77. Lin FR, Niparko JK, Ferrucci L (2011) Hearing loss prevalence in the United States. *Arch Intern Med* 171(20):1851–1852.
78. Florentine M, Buus S, Scharf B, Zwicker E (1980) Frequency selectivity in normally-hearing and hearing-impaired observers. *J Speech Hear Res* 23(3):646–669.
79. Doherty KA, Lutfi RA (1999) Level discrimination of single tones in a multitone complex by normal-hearing and hearing-impaired listeners. *J Acoust Soc Am* 105(3):1831–1840.
80. Buran BN, et al. (2014) A sensitive period for the impact of hearing loss on auditory perception. *J Neurosci* 34(6):2276–2284.
81. de Villers-Sidani E, et al. (2010) Recovery of functional and structural age-related changes in the rat primary auditory cortex with operant training. *Proc Natl Acad Sci USA* 107(31):13900–13905.
82. Naber M (2008) Soundgen: A Web services based sound generation system for the psychoacoustics laboratory. MS thesis (Massachusetts Institute of Technology, Cambridge, MA).
83. Levitt H (1971) Transformed up-down methods in psychoacoustics. *J Acoust Soc Am* 49(2):Suppl 2:467.
84. Killion MC, Niquette PA, Gudmundsen GI, Revit LJ, Banerjee S (2004) Development of a quick speech-in-noise test for measuring signal-to-noise ratio loss in normal-hearing and hearing-impaired listeners. *J Acoust Soc Am* 116 (4 Pt 1):2395–2405.
85. Guo W, et al. (2012) Robustness of cortical topography across fields, laminae, anesthetic states, and neurophysiological signal types. *J Neurosci* 32(27):9159–9172.