



Sound localization in a changing world

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In natural environments, neural systems must be continuously updated to reflect changes in sensory inputs and behavioral goals. Recent studies of sound localization have shown that adaptation and learning involve multiple mechanisms that operate at different timescales and stages of processing, with other sensory and motor-related inputs playing a key role. We are only just beginning to understand, however, how these processes interact with one another to produce adaptive changes at the level of neuronal populations and behavior. Because there is no explicit map of auditory space in the cortex, studies of sound localization may also provide much broader insight into the plasticity of complex neural representations that are not topographically organized.

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Introduction

In order to maintain accurate and efficient representations of a continuously changing world, the brain must possess a considerable degree of flexibility, updating neuronal response properties to reflect current behavioral goals and sensory conditions. A fundamental goal of neuroscience is therefore to explore the processes — including the cellular mechanisms — that underlie this flexibility, with the aim of improving our understanding of the neural basis of perception in real-life situations. Moreover, exploiting the dynamic nature of sensory processing is key to promoting the recovery of function in individuals with sensory impairments.

Because there is no representation of auditory space in the cochlea, sound localization provides an excellent model system for studying these issues within the context of a computationally demanding aspect of

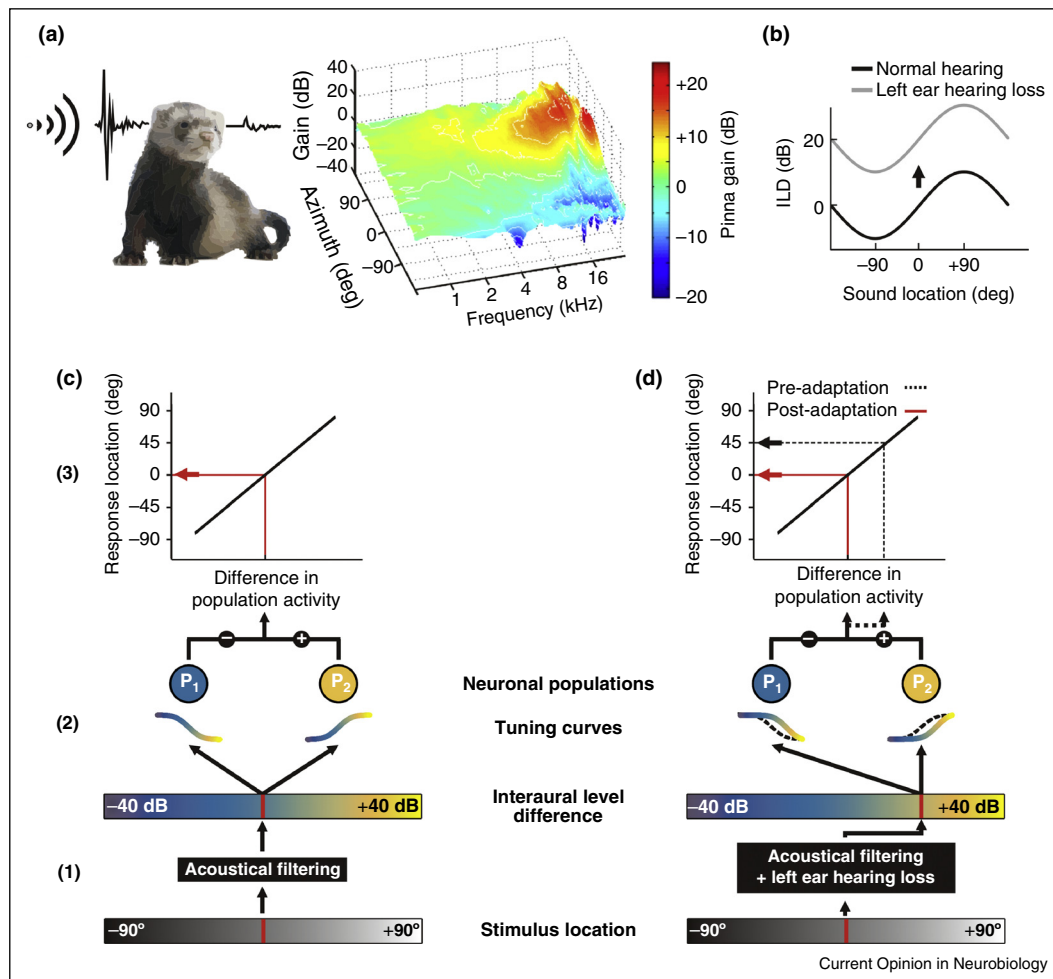
neural coding. Spatial hearing plays a critical role in many species, not simply for determining the location of sound sources, but also for segregating different sources in acoustically complex environments. Moreover, the diversity of such environments, coupled with the prevalence of many forms of hearing loss [1], mean that there is considerable adaptive pressure on spatial hearing throughout the lifespan. Studies of sound localization can therefore provide valuable insights into the plasticity of ecologically important aspects of sensory processing.

Plasticity and context-dependent processing

In recent years, studies of sound localization have provided considerable evidence to support the view that neural processing is rapidly updated to reflect changes in sensory conditions. An excellent example of this is provided by the finding that the influence of sound location on the responses of forebrain neurons increases when multiple sounds are present [2,3] or when a localization task is carried out [4,5]. The existence of context-dependent coding raises a number of wider issues relevant to the study of neural plasticity, including (i) the extent to which such processing is learned and (ii) the importance of measuring plasticity in the appropriate environmental or behavioral context.

As with many other sensory functions, sound localization relies on the ability to integrate information provided by different sensory cues [6]. These cues include differences in the level and timing of inputs to the two ears (interaural level differences, ILDs; interaural time differences, ITDs) and monaural spectral cues, which require the detection of specific spectral features imposed on sounds by the direction-dependent filtering effects of the head and ears (Figure 1a,b). The challenge faced by the brain is therefore to interpret binaural and monaural cues correctly and combine them in an efficient manner to accomplish specific goals. To do this, the brain must learn (i) the relationship between individual spatial cues and stimulus location, particularly during development when that relationship is changing as a result of head and ear growth, (ii) how much weight particular cues should be given when making localization judgments, and (iii) how to adjust spatial processing to reflect non-auditory factors, including behavioral goals and the availability of information from other sensory modalities. Using sound localization as a specific example, we propose that sensory processing in a changing world involves modifying one or more of these stages over multiple timescales, and that this is likely to emerge from dynamic interactions between cortical and sub-cortical mechanisms.

Figure 1



Remapping of altered sound localization cues in the brain. (a) When a sound is presented, the filtering effects of the head and ears alter the sound waveform separately for each ear (left). This generates direction-dependent monaural spectral cues (right), interaural level differences (ILDs) and interaural time differences. (b) Variation in ILDs with sound location. Positive values indicate locations on the right side of space, which under normal hearing conditions correspond to positive (i.e. right-ear greater) ILDs (black line). Monaural occlusion shifts the range of binaural cues experienced (effect of left-ear hearing loss on ILDs is shown by the gray line), but leaves the spectral cues provided to the non-deprived ear intact. (c) (1) Under normal hearing conditions, a sound presented at 0° (directly in front of the subject) will produce an ILD of approximately 0 dB (equal intensity in the two ears) due to the acoustical filtering of the head and ears. These values are indicated within each scale bar by a vertical red line. (2) The ILD is converted into a specific pattern of population activity, which is determined by the ILD preferences (i.e. the tuning curve) of each neuron. In mammals, neurons are typically broadly tuned to a single side of space. A simple population code for auditory space can therefore be created by calculating the difference in mean activity between two sub-populations of neurons with opposing ILD preferences (P_1 , P_2 ; denoted by colored circles). Sample tuning curves for neurons belonging to each subpopulation are shown immediately below, which depict the firing rate as a function of ILD. (3) A specific difference in activity between the two subpopulations corresponds to a particular response location. (d) When a hearing loss is experienced in the left ear, the mapping of sound location onto ILD is shifted (in this case toward more positive ILDs). Prior to adaptation of their tuning curves (dashed black lines), the difference in the responses of P_1 and P_2 will lead to systematic errors in response location. Following adaptation (colored lines), tuning curves are shifted to compensate for the effects of the hearing loss, which restores the correct relationship between population activity and response location.

Spatial cue remapping

A popular approach to studying the plasticity of auditory spatial processing has been to reversibly alter the relationship between stimulus location and the binaural cues available. This can be easily achieved by occluding one ear so that the acoustical input is attenuated and delayed, thereby changing the ILD and ITD values corresponding

to each direction in space. Using this approach, Knudsen and colleagues [7,8] found that developing barn owls adapt to the abnormal binaural cues, with neurons shifting their sensitivity to these cues in a way that compensated for the effects of monaural occlusion. Recent work has shown that mammals also possess the ability to developmentally remap spatial position onto abnormal ILDs,

which can be observed both behaviorally and in the responses of neurons in the primary auditory cortex (A1) [9^{*}] (Figure 1b–d).

As with other sensory functions, monaural deprivation experiments indicate that critical periods exist for the maturation of binaural hearing [8,10^{*},11]. Similarly, early onset deafness limits the capacity of humans and other species to fully exploit binaural cues if bilateral cochlear implantation is carried out in adulthood [12–14]. The benefits for spatial hearing in children also increase if the interval between implantation of each ear is kept to a minimum [15]. Nevertheless, the capacity to accommodate altered spatial cues is not restricted to development, since adult humans can learn to localize accurately using altered binaural [16,17] or spectral localization cues [16,18,19,20^{*},21]. This adaptive strategy therefore appears to be widely shared, both across species and — at least in mammals — in adulthood as well as during development. But while barn owls reared with monaural occlusion show systematic localization errors when normal hearing is restored, no aftereffect is seen in adult humans following adaptation to altered spatial cues [16,18,19,20^{*},21], implying that different sets of spatial cues can be mapped onto the same locations.

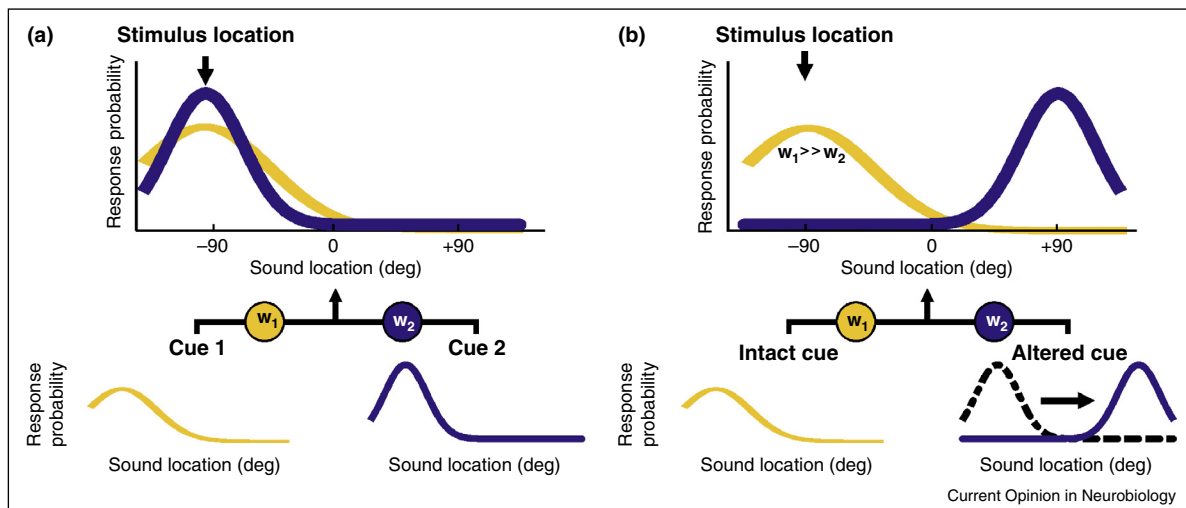
The effects of long-term changes in spatial cues are paralleled — albeit much more rapidly — by changing the stimulus statistics that immediately precede a target

sound. In particular, neuronal ILD and ITD sensitivity, and the perception of auditory space in human listeners, can temporarily change according to the statistics of the preceding stimulus distribution [22,23,24^{*}]. One interpretation of this is that the auditory system may care more about relative sound location than it does about the actual position of a sound source, perhaps reflecting variations in the range of cue values experienced at fast timescales and, to a lesser extent, across different soundscapes [25]. Recent work, however, suggests that the absolute position of a sound source may be preserved in the neural response to the onset of a stimulus [26^{*}]. The auditory system could therefore retain this information by focusing to a greater degree on stimulus onset, which is supported by behavioral studies in humans [27].

Spatial cue reweighting

In situations where some, but not all, of the spatial cues are altered, an alternative form of plasticity to cue remapping is to down-weight the spatial information provided by the altered cues and instead rely more on the cues that remain intact. For example, in the specific case of monaural hearing loss, a number of studies have shown that sound localization behavior in mammals adapts both during development and adulthood by giving greater weight to the unchanged monaural spatial cues provided by the normally hearing ear [28–30,31^{**}] (Figure 2). In ferrets raised with one ear occluded, this behavioral reweighting of spatial cues is paralleled by corresponding changes in A1 [31^{**}]. Surprisingly, however, the relative

Figure 2



Reweighting of auditory spatial cues. (a) Under normal hearing conditions, the pattern of localization responses elicited by different spatial cues (yellow and blue) may be similar (bottom; response probability is plotted as a function of sound location for each cue). Combining these cues therefore produces similar responses, irrespective of the relative weight (w_1 , w_2) given to each cue (top). (b) When one of the cues is altered, as with interaural level differences following monaural deprivation (blue), behavioral responses guided by that cue will initially be shifted toward incorrect locations (bottom). However, if another cue — in this case, the spectral shape information available at the non-occluded ear — remains intact (yellow), these incorrect responses can be mitigated, or avoided entirely, by increasing the relative weight given to that cue ($w_1 \gg w_2$; top). Cue reweighting can therefore contribute to adaptation when some, but not all, spatial cues are altered by the hearing impairment.

weight given to different cues is not fixed, but rather depends on the prevailing sensory conditions. In particular, monaurally deprived animals that have become more dependent on monaural spatial cues for localization in the horizontal plane rapidly revert to using binaural cues whenever the earplug is removed [31^{••}]. As with the effects of spectral cue manipulations in adult humans, there is therefore no aftereffect when normal hearing is restored, ensuring that accurate sound localization can be maintained under different hearing conditions.

One explanation for these results is that the weight given to different cues depends on their relative reliability, a strategy that is optimal if certain conditions are met [32]. Under normal hearing conditions, binaural cues provide more accurate and reliable information than monaural cues about the location of sounds in the horizontal plane, and therefore dominate both behavioral and neuronal responses. In contrast, when binaural cues are degraded by monaural occlusion, the spectral cues available at the contralateral ear may provide relatively more accurate spatial information and are therefore given correspondingly greater weight. This type of reliability-based cue reweighting has been extremely successful in characterizing the integration of multisensory cues [32]. Similar principles have also been used to model sound localization in humans [33] and to account for the relationship between sound frequency and ITD selectivity in the barn owl midbrain [34]. However, since cue reliability can vary across different acoustical contexts, prior experience may play a crucial role in determining the set of weights used at any given moment in time [31^{••}].

Although distinct weighting strategies could be distributed across separate populations of neurons, individual neurons can use different aspects of their response to multiplex sensory information, including different auditory spatial cues [35] and both spatial and non-spatial stimulus attributes [36]. This means that a common set of neurons could potentially employ different weighting strategies. Similarly, since cue remapping and cue reweighting are used to adapt to asymmetric hearing loss in the same individuals [9[•],31^{••}], it is possible that both of these adaptive processes could contribute to adaptation in spatial sensitivity of the same neurons.

Importance of behavioral context

In addition to adapting to changes in the localization cues available, auditory spatial processing can be refined in situations where its behavioral importance is increased, even if the acoustical inputs remain the same. Behavioral studies in ferrets [37] and humans [38] have shown that training-induced improvements in spatial processing are specific to individual binaural cues, though cue specificity may be asymmetric, with one study showing that ILD training generalizes to an ITD task but not vice versa [38]. How much plasticity is observed may also depend on the

stimuli used [37,39]. A neural correlate of these learning effects has been demonstrated in rat A1, where the spatial tuning of the neurons is sharpened, in conjunction with local changes in NMDA and GABA_A receptor subunit expression, as behavioral performance improves with training [40].

Training in adulthood can even reverse the negative impact of abnormal developmental experience on sound localization accuracy and A1 responses [41,42], and can improve sound localization performance in hearing-impaired clinical populations [43]. Similarly, training juvenile animals has been shown to enhance non-spatial auditory abilities in adulthood [44] and offset the perceptual deficits caused by hearing loss during development [45]. Although training-dependent plasticity often takes place relatively slowly, recent work in humans indicates that feature-specific learning can occur rapidly in a task that requires spatial processing, which may reflect top-down biasing of cortical regions thought to be particularly involved with sound localization [46]. Nevertheless, carrying out a sound localization task does not necessarily sharpen spatial tuning in auditory cortex [47[•]], which may only occur if the spatial aspect of the task is perceptually challenging [4]. Conversely, it is unclear to what extent training is strictly necessary for the adult plasticity of spatial hearing, since non-spatial aspects of auditory processing can be altered through prolonged passive exposure to environmental sounds [48]. A key goal for future research is therefore to better understand the interaction between sensory plasticity and behavioral context and how this varies throughout the lifespan.

Neural origins of auditory spatial plasticity

Evidence for training-dependent plasticity of cortical processing is consistent with the findings reviewed above that both spatial cue remapping and reweighting by A1 neurons can account for the adaptive changes in sound localization behavior exhibited by monaurally deprived ferrets [9[•],31^{••}]. However, a more direct link between cortical physiology and behavior has been provided by the demonstration that pharmacologically deactivating different auditory cortical areas disrupts the ability of adult ferrets to adapt with training to asymmetric hearing loss [49]. Moreover, lesioning cholinergic neurons in the basal forebrain that target the auditory cortex also impairs this learning process [50], adding to the growing evidence for the role of neuromodulatory inputs in regulating the excitability of auditory neurons [51] and in enabling both plasticity of mature cortical circuits and enhancement of perceptual abilities [52].

In the visual system, there is evidence that perceptual learning primarily involves changes in stimulus selectivity or in the readout from neurons in higher-level, task-relevant cortical areas, such as MT or V4 [53]. In contrast to the visual system, auditory training results in more

extensive plasticity at earlier stages of the cortical hierarchy, including A1 [54]. Moreover, A1 activity represents not only the acoustical properties of the stimulus, but also the behavioral relevance [55] and choice [56,57] made by the animal. Nevertheless, behavioral modulation of cortical responses has been found to be greater in higher-order auditory areas than in A1 [58,59], and it seems likely that this will also turn out to be the case for the longer-term effects of task-specific experience.

Because sensitivity to auditory localization cues arises in the brainstem, plasticity in spatial processing is not necessarily restricted to the cortex. Indeed, sensory experience plays a critical role in the development of the auditory space map in the mammalian superior colliculus (SC) [60] and its avian homologue [7]. However, while monaural deprivation affects the development of binaural response properties in the inferior colliculus (IC), larger changes are seen in the cortex [11], which appears to provide the primary substrate for plasticity throughout the lifespan. Nevertheless, there is growing evidence that the interplay between cortical and subcortical processing may underpin experience-dependent plasticity in the perception of speech [61,62,63] and sound-source location [64]. In particular, corticofugal modulation may be responsible for adjusting responses to behaviorally relevant sound features, both during learning [63,64] and as the stimulus statistics change [65].

Recent evidence has also highlighted the involvement of commissural connections in shaping some of the response properties of neurons in the IC [66] and cortex [67]. Since these connections have been implicated in spatial processing [68], it is possible that commissural modulation, either subcortically or at higher levels of the auditory pathway, could contribute to the adaptive plasticity that results from monaural deprivation. Corticostriatal plasticity also helps link particular acoustical inputs with behavior [69], and this may be important for guiding appropriate responses following changes in auditory spatial cues.

Visual influences on auditory spatial plasticity

Sound sources are often visible as well as audible and the availability of visual information can improve the accuracy of sound localization estimates [70], and even help to suppress echoes that are an inevitable consequence of listening in reverberant environments [71]. Binaural cue discrimination is also enhanced if subjects look toward the sound while keeping their head still [72], adding to the physiological evidence that eye position signals can modulate activity in the auditory system [73]. Another recent study failed to find an effect of eye position on human auditory cortical responses, but did show that responses to task-irrelevant sounds can be influenced by transient changes in attended visual stimuli that predict the timing of sound onset [74].

Not surprisingly, auditory localization abilities can be altered if vision is impaired. The most commonly reported finding is that some blind individuals show superior auditory spatial perception relative to sighted controls [75,76,77]. Interestingly, as with adaptation to a unilateral hearing loss, more accurate sound localization in blind humans is associated with greater dependence on spectral localization cues [78]. However, in blind subjects, this superior use of spectral cues for localization in the horizontal plane appears to come at the cost of a reduced ability to use these cues for localization in the vertical plane [79]. More complex aspects of spatial hearing are additionally impaired following loss of vision [80]. These disparate effects of blindness on auditory localization undoubtedly reflect methodological differences between studies, but may also represent a balance between (i) the lifelong influence of vision in calibrating neural representations of auditory space [81] and (ii) the compensatory crossmodal plasticity that follows visual deprivation and increased dependence on hearing for spatial navigation [82].

Because of the influence that vision can have on sound localization, it might be expected that the capacity to accommodate altered auditory spatial cues would be affected by the presence or absence of visual information. However, humans can learn to use modified spectral cues to make elevation judgments both within and outside the visual field [19], supporting a previous finding that adult ferrets can adapt to asymmetric hearing loss without visual feedback [29]. It has been proposed that accommodation to altered spatial cues can be achieved by unsupervised sensorimotor learning through experience of the dynamic acoustic inputs associated with an individual's own movements [83]. Indeed, encouraging human subjects fitted with pinna molds to make exploratory head movements in order to maximize audio-motor feedback has been found to improve the rate and extent of adaptation to altered spectral cues [18]. How active movements promote auditory spatial learning is unclear, but it is interesting to note that motor-related signals originating in the secondary motor cortex can alter auditory cortical activity [84].

Although visual information is not required for learning new associations between auditory spatial cues and directions in space, it does appear to facilitate this process. Thus, synchronous audiovisual training enhances the recovery of accurate sound localization by human subjects wearing a unilateral earplug [85], and improves the perception of spectrally degraded speech by listeners with normal hearing [86]. These findings suggest that it might be beneficial to combine visual and auditory cues in the rehabilitation of the hearing impaired. However, audiovisual training appears to impede auditory speech learning in pre-lingually deaf individuals who receive cochlear implants later in life, presumably because of their greater

dependence on visual speech perception than normal-hearing subjects [87]. Nevertheless, a different result has been obtained in adult ferrets fitted with bilateral cochlear implants following deafening in infancy [14]. These animals were initially unable to localize sound even after multiple auditory training sessions, but showed a considerable and persistent improvement in performance following a training paradigm in which auditory and visual stimuli were randomly interleaved. Moreover, the auditory responsiveness of A1 neurons and their sensitivity to ILDs, the principal spatial cue available to bilateral cochlear implant users, was significantly enhanced in these animals compared to ferrets that did not experience the crossmodal training paradigm [14]. The brain regions mediating this crossmodal transfer of localization training are unknown, but it seems likely that frontal cortical areas are involved [88].

Future directions

Understanding the interplay between dynamic processing of sensory information at multiple timescales, and at different levels of processing, is an important and largely unexplored area of neuroscience. Thus, while neural processing can be rapidly updated to reflect changes in stimulus statistics or behavioral goals, it is likely that this capacity is facilitated by learning [63^{*}]. For example, mechanisms that enable the auditory cortex to maintain robust representations of natural sounds in noisy and reverberant environments [89,90] may require subjects to learn which aspects of the acoustical input, such as room echoes, are important or not in specific behavioral and environmental contexts [91,92].

Although the adaptability of sound localization has been studied primarily by looking at changes in the response properties of individual neurons or small multi-unit clusters, a key challenge for future work is to understand how population codes change at various stages of processing as a function of sensory experience and behavioral goals. For example, the spatial sensitivity of a relatively small proportion of the neurons recorded in different cortical areas is affected when cats carry out an auditory task, implying that a specific subset of the neuronal population may be particularly important during behavior depending on the stimulus or task involved [4]. Similarly, studies of sound localization in complex or abnormal hearing conditions can provide further constraints for deciding between candidate population codes, with recent work highlighting the importance of neuronal heterogeneity within each hemisphere for representing sound source location [9^{*},93–95].

There is growing evidence that the structure of population codes may vary between the midbrain and forebrain [96–98], and it has been suggested that this may reflect differences in the behaviors that are guided by different levels of the auditory pathway [96]. If this is the case, then

we might expect population responses to also vary as a function of sensory experience and behavioral goals. Although relatively few studies have explored the effects of prior experience on population coding of auditory space [9^{*}], learning of a non-spatial auditory task is associated with a change in the correlational structure of population coding in birds [99^{**}]. By linking such changes with behavioral improvements, plasticity studies provide a powerful approach for deciphering the nature of population codes for sound location. Since there appears to be no explicit map of auditory space in the cortex, such studies could also provide fundamental insight into the general nature of complex cortical representations that are not topographically organized. In addition to their intrinsic scientific and clinical importance [1], studies of sound localization in a changing world may therefore help us understand much wider aspects of neural function.

Conflict of interest statement

Nothing declared.

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