

New perspectives on the owl's map of auditory space

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A map of sound direction was found in the owl's midbrain more than three decades ago. This finding suggested that the brain reconstructs spatial coordinates to represent them.

Subsequent research elucidated the variables used to compute the map. Here we provide a review of the processes leading to its emergence and an updated perspective on how and what information is represented.

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Introduction

The barn owl's midbrain contains maps of auditory space (MASPs) in two interconnected structures: the external nucleus of the inferior colliculus (ICX) [1] and the optic tectum (OT) [2]. The existence of MASPs in the midbrain is not unique to barn owls. It has been described in several other species (rodents, ferret, cat, monkey) [3–6]. However, the resolution and the topographic precision of the MASPs in barn owls exceed those of any other species studied.

Mapped representation of space in egocentric coordinates is a common feature in the somatosensory and visual systems. The finding that the auditory system possesses an equivalent representation of space puts it at an even level. However there is a fundamental difference between the MASP and the retinotopic/somatotopic maps. In the latter, the basic structure of the maps results from the peripheral representation of the sensory information, which is topographic by nature, whereas the former emerges by an elaborate computational process that transforms information of frequency and time into a two-dimensional map of space. Hence, the MASP is considered a fine example of a computational map [7] and since its discovery in 1978 [1] it has served as a model system to study the neural processing involved in the

computation, representation and calibration of brain maps.

The synthesis of a two-dimensional MASP involves several steps (Figure 1). In the first stage each dimension — vertical and horizontal — is computed from frequency-specific neurons; subsequently, both dimensions are combined into space-specific neurons, that is, neurons that are narrowly tuned to space. To form a map, the space-specific neurons have to be arranged in the brain with their preferred-direction being laid systematically along the spatial axes. In the barn owl this stage is partly developmentally regulated and partly achieved by experience dependent learning. In this review we will first address how the auditory map emerges and theories of how space is represented; then we will discuss the integration of the MASP into a multimodal saliency map in the OT that controls orienting responses.

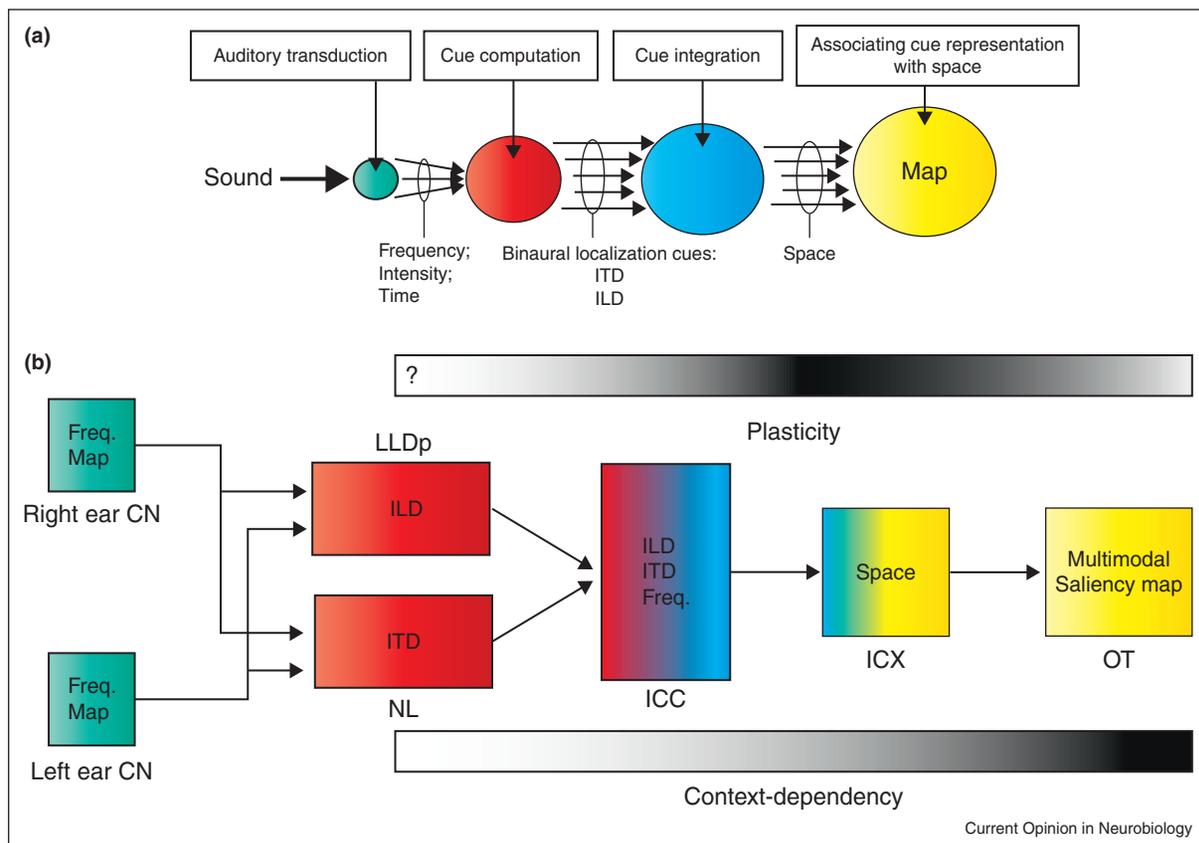
Emergence of a map of auditory space

In owls, the auditory spatial cues that result from comparing the inputs to each ear, the interaural time difference (ITD) and interaural level difference (ILD) are orthogonalized by an ear asymmetry. ITD remains correlated with the horizontal coordinate, like in other species, whereas ILD varies with elevation [8,9]. Each cue is computed and processed in parallel pathways [10] that converge one stage before the MASP first emerges in ICX [11,12]. Combination selectivity to ITD and ILD results in the sharp spatial tuning of ICX neurons [13•].

Topography is already present in stages of the pathway that represent the horizontal and vertical coordinates, that is, the ITD and ILD pathways. A dorsoventral gradient of inhibition yields a primordial map of ILD in lemniscal nuclei [14,15] whereas organized delay lines underlie the emergence of a map of ITD in the pontine nucleus laminaris [16,17]. This topography carries over to the midbrain [18•]. At ICX as well, further processing takes place that enhances spatial tuning and removes ambiguity [13•,19,20]. It is assumed that the integration of the ITD and ILD streams preserves each pathway's topography in perpendicular dimensions of the MASP.

Although ITD and ILD alone are sufficient to drive orienting behavior [8,21], owls as well as mammals can also rely on spectral cues for locating and identifying sound sources in space [22,23]. It has been shown that midbrain space-specific neurons display frequency dependent tuning to ITD and ILD [24,25]. Whether this

Figure 1



The formation of the owl's auditory map of space. **(a)** An illustration of the four steps required to create an auditory map of space (see upper text) and the information obtained at each step (see lower text). **(b)** An illustration of a selected part of the auditory pathway leading from the cochlear nuclei to the MASP in the OT. Boxes indicate brain structures and the text inside the boxes relate to the main type of information represented. The colors code the processing steps as displayed in the inset. The upper gray bar designates the hypothetical profile of experience-dependent plasticity along the pathway; black symbolizes sites which demonstrate high levels of experience-dependent plasticity and white low levels. The question mark indicates a site where it is not known to what extent plasticity takes place. The lower gray bar designates the hypothetical profile of context-dependency along the pathway, black symbolizes areas whose neural responses depend on stimulus context (history, distracters, among others) and vice versa. *Abbreviations* – Freq.: frequency; ITD: interaural time difference; ILD: interaural level difference; CN: cochlear nucleus; LLDp: dorsal nucleus of the lateral lemniscus posterior; NL: nucleus laminaris; ICC: central nucleus of the inferior colliculus; ICX: external nucleus of the inferior colliculus; OT: optic tectum.

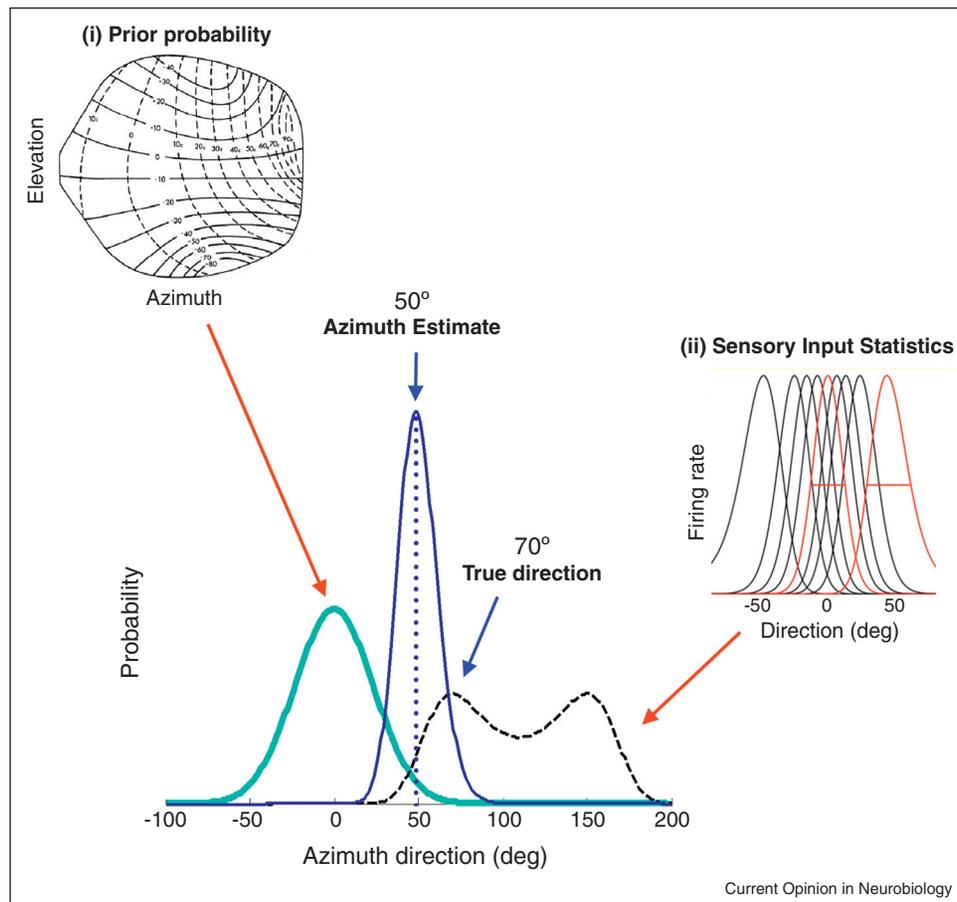
means neurons are tuned to the space-dependent spectral filtering of the head remains to be demonstrated.

The code in the map

The presence of a map, where a map was unexpected, constituted strong evidence in support of topography ('place') as a language of the brain. Along this line, focal lesions of the MASP in owls caused temporary inability to localize sounds in areas of space corresponding to the location of the lesions [26]. In addition, microstimulation studies related location in the map to goal-oriented motor commands, where stimulation caused head- and eye-orienting responses toward the area of space represented in the stimulated region [27,28]. Low intensity microstimulations also primed behavioral responses to auditory stimuli coming from the represented direction more than from other directions [29*].

The response of neurons of the MASP has been related to behavioral sensitivity and accuracy in the owl's sound localization. The ability to resolve ambiguous stimuli was correlated with single-neuron responses [30,31]. In addition, the owl's minimal-angle discrimination could be predicted by the shape of individual cells' spatial receptive fields [32*]. However, to what extent is a single position of the map or the activity of the entire population taken into account to infer sound direction is an open question. Recent work has reformulated the idea of place coding in the owl's midbrain. This work provided a solution to the neural representation and localization behavior, which displays higher frontal accuracy and a systematic underestimation in the periphery observed in owls and other species [2,33–36]. It was shown that if natural statistics were encoded in the over-representation of frontal space and in the

Figure 2



Statistical inference in the owl's sound localization pathway. Probability distributions as a function of azimuth of the owl's estimate of sound direction (blue), prior probability (light blue) and statistics about the sensory input (dashed black) for a sound source located 70 degrees away from the front (true direction). The estimate of azimuth direction (blue) results from combining the prior (light blue) with the statistical relationship between the sensory input and the environment (dashed line). Direction is underestimated for locations away from the center matching the owl's behavior [33]. Prior information is encoded in the inhomogeneous distribution of preferred directions in the optic tectum (i inset), where frontal space is overrepresented [2]. Sensory input statistics are represented by the inhomogeneous tuning-curve widths in the optic tectum (ii inset), where curves in the front are narrower than in the periphery (red curves with horizontal bars). Modified from [37**].

progressive broadening of spatial tuning in the periphery, a population vector could approach Bayesian inference [37**]. (Figure 2).

Is sound direction alone mapped in the MASP? Lateral connections in neural maps allow for detecting context-dependent stimulus features. Already at the level of ICX, neurons are selective to sound motion [38] and suppress responses to echoing sounds [39*]. Because the map is not uniform, for example, there are more neurons dedicated to frontal space [2], lateral connectivity is likely biased. A surround-suppression bias has been found, superimposed to the MASP, which could be related to the heterogeneous spatial tuning of the population [40]. The dependence on context is further elaborated in the tectal MASP (see below).

Experience-dependent alignment of visual and auditory space maps

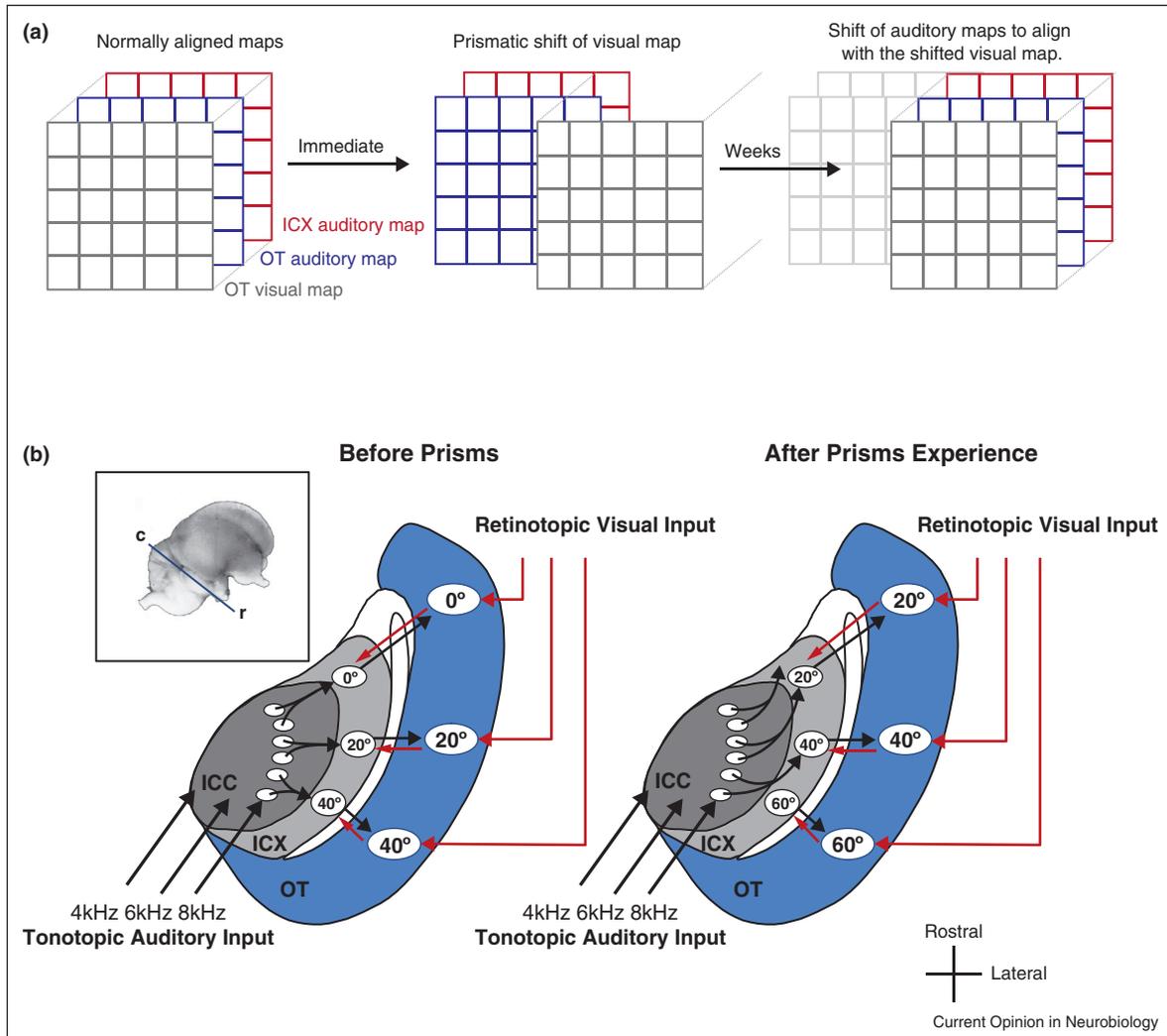
The MASPs of both the ICX and OT are highly vulnerable to experience-dependent plasticity, particularly at young age before sexual maturity [41–44]. Both maps undergo dramatic reorganization as a result of long-term manipulations of the auditory sense (by ear plugs [41]) as well as of the visual sense (by prismatic spectacles [42]). That an auditory manipulation induces adaptive realignment of RFs [41] is expected and intuitive. But why would a visual manipulation results in a reorganization of the MASPs without changes in the visual map of space [45]? The answer, most likely, is that for a unified perception it is essential that internal representations of auditory and visual spaces be matched. A neural-correlate of this matching may be

found in the alignment of the auditory and visual maps in the OT, that is, visual and auditory signals arising from a particular direction in space are represented in the same site and co-vary with the anatomical location of the neurons. Therefore any shift from the normal alignment between modalities (as brought about by the prisms effect) triggers plasticity that restores alignment. Indeed, prismatic experience in barn owls results in a

systematic shift in auditory RFs, which realigns them with the visual RFs (Figure 3) [45].

Alignment can be achieved either by shifting the auditory, visual or both maps. Evidence from barn owls and other species supports the notion that it is the auditory map that is plastic; changing to align with the visual map which serves as a template [42,46,47]. Considering the

Figure 3

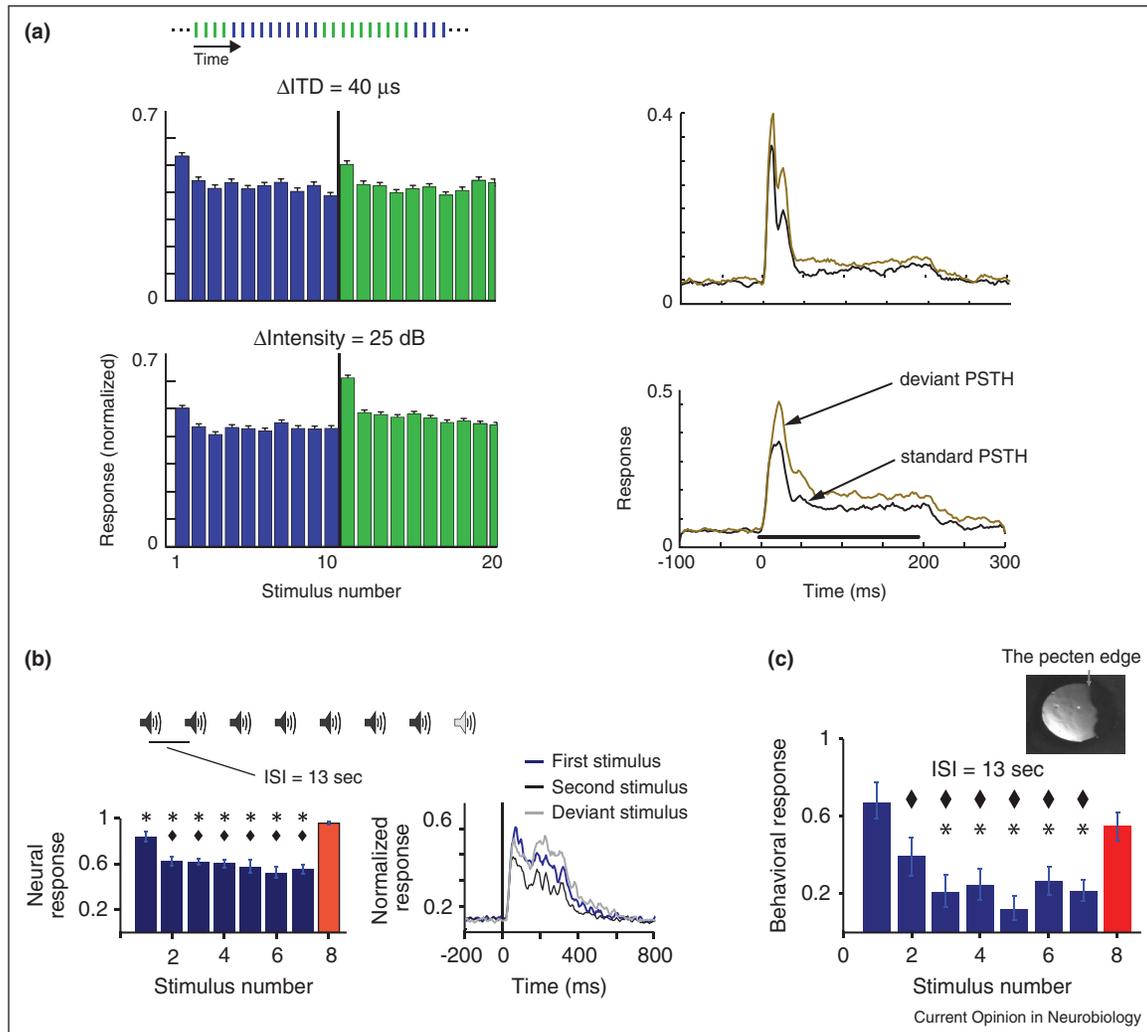


Schematic summary of the changes that occur in the midbrain representation and anatomy as a result of adaptation to prisms. **(a)** In a normal barn owl all maps are aligned (illustrated on the left). Because barn owls lack eye movements, prismatic spectacles lead to a chronic displacement of the image on the retina and as a result a shift of the visual map. During the course of experience with the prisms the auditory maps move in the brain to align again with the visual map (illustrated on the right). **(b)** The main figures depict a horizontal section through the right tectal lobe. The inset shows a lateral view of the barn owl's entire brain (r, rostral; c, caudal). The line marks the approximate plane of the section. In the central nucleus of the inferior colliculus (ICC), auditory localization cues are represented in frequency-specific channels. Information across frequencies is then integrated by neurons in the external nucleus of the inferior colliculus (ICX) to create space-specific auditory neurons that are organized to form a map of contralateral space. This map is in turn projected through topographic connections to the optic tectum (OT), where it joins the visual retinotopic map arriving from the retina and forebrain. Topographic projections back from the OT to the ICX are thought to carry visual spatial information to instruct auditory plasticity in the ICX. The circled numbers in the ICX and OT represent the azimuthal angles in space to which the neurons are tuned. Following a period of several weeks of experience, during early life, with prisms that shift the scene by 20 degrees to the right, the axonal connections between the ICC and the ICX grow in an abnormal pattern (right figure). Connections are shifted rostrally on the right side of the brain accompanied by a caudal shift of connections on the other side of the brain (not shown). This pattern of axonal regrowth shifts the auditory maps in both the ICX and the OT so that they realign with the shifted visual map.

fact that the MASP is computational, depending critically on precise integration of information from the two ears across frequency bands, it makes sense for the visual map to guide the MASP and not the other way around.

The site of visually guided auditory plasticity has been identified in the ICX (Figure 3b). Prism-induced changes in auditory spatial tuning are brought about by rewiring inputs from the central nucleus of the inferior colliculus to

Figure 4



Neurons in the OT are sensitive to the history of stimulation in a manner resembling habituation of the orienting reflex. **(a)** The histograms show the average response of a population of neurons in the OT to a long sequence of stimuli (200 stimuli). The duration of each stimulus was 200 ms and the inter-stimulus interval (ISI) was 1 s. The sequence was alternating between two different stimuli, every 10 repetitions the stimulus was switched (sequence is illustrated in inset). The upper row shows results from experiments where the two stimuli differed only by the ITD values. The lower row shows results from experiments in which the two stimuli differed only by their intensity. One stimulus (blue bars) was softer compared to the other (green bars). The post stimulus time histograms (PSTHs) on the right compare the average response to one stimulus when it was first in a row (deviant) with the response to the same stimulus when it was last in the row (standard). It can be seen that trials in which the stimulus was deviant compared to its past elicited stronger responses. Modified from [60*]. **(b)** The memory of adaptation in the OT is several seconds long. The histogram shows the average response of neurons in the OT as a function of the position of the stimulus in a sequence with an ISI of 13 s. The sequence was composed of seven repetitions of the standard sound followed by one presentation of an odd sound (see inset). The blue bars designate responses to the seven repeated presentations of the standard stimulus and the red bar designates the response to the last odd stimulus. Error bars indicate SEMs. Diamonds indicate responses that were significantly smaller than the response to the last odd stimulus. Asterisks indicate responses that were significantly smaller than the response to the first stimulus. The graph on the right shows the average PSTH curve of the response to the first stimulus (thick dark curve) compared to the average PSTH curve of the second stimulus (thin dark curve) and the average PSTH curve of the response to the last odd stimulus (gray curve). **(c)** The inset displays a video frame showing the infra-red light reflected through the pupil from the right eye. The edge of the pecten oculus, a retinal landmark used to track minute eye movements is marked by the arrow. The histogram shows the average reflexive eye shift to a sequence of 8 auditory stimuli of which the eighth stimulus was odd. The blue bars indicate the responses to the seven repeated presentations of the same standard stimulus. The red bar shows the average response to the last odd stimulus. Note the similarities between the neural responses in B and the behavioral responses in C. Panels B and C modified from [61].

the ICX [43]. The OT projects topographically back to the ICX [48,49] giving rise to visual signals that presumably instruct auditory plasticity by ways of Hebbian learning [50,51*,52]. Having the site of plasticity at the level of inputs to the ICX, where information converges across frequencies, allows for frequency specific shifts in spatial RFs. Such specific shifts have been demonstrated in the MASP by manipulating the acoustic space with passive filtering devices [41]. The tectal MASP then inherits the plastic changes from the ICX MASP, embedding the auditory input in a multimodal, context-dependent, sensory-motor map.

Mapping saliency of the auditory scene

The OT in barn owls, like its homologue the SC, contains a motor map of gaze directions [27] and is considered part of the gaze control system. However, evidence from numerous studies, mostly in primates and cats, demonstrates that, in addition to coordinating movement, the gaze control system is involved in the selection of the most relevant visual target for behavioral response [53–59]. What about the selection of auditory targets? Is the MASP in the OT coding saliency to support auditory stimulus selection? It was recently shown that neurons in the tectal MASP are robustly sensitive to probability, preferring stimuli that are rare and unexpected [60**]. Thus, for example, a weak auditory stimulus can elicit tectal responses that are stronger than responses elicited by a 25 dB louder stimulus if the weak stimulus is presented scarcely and the loud stimulus is more common (Figure 4a) [60**]. This feature was, however, not observed in the ICX MASP [60**]. Auditory responses in the tectal MASP undergo adaptation with relatively long memory; a single, short and weak stimulus can significantly reduce the response to the same stimulus if presented up to a minute later [61]. This long term adaptation, as in habituation, was stimulus specific (Figure 4b,c) and first emerged in OT [61].

Auditory responses in OT are not only modulated by stimulus history but also by simultaneous competitive stimuli. Mysore and colleagues studied cross modal lateral interactions and showed that the responses to auditory stimuli are reduced in the presence of visual distracters and vice versa [62**]. This lateral inhibition was global, covering the entire frontal space [62**]. Moreover, they identified a unique ‘switch like’ interaction in which neurons code the relative saliency between two competing stimuli [63,64], a property that may facilitate the selection of the most salient stimulus. In addition it was shown that microstimulation in the arcopallium gaze field (AGF), a forebrain area equivalent to the frontal eye fields [65], changed auditory responses in OT in ways that resembled top-down modulation by spatial attention [66**]. Such connections constitute a network through which task-related information can influence saliency mapping in the OT [66**].

Given the well established role of the OT in gaze control it is not a surprise that electrical microstimulation in the OT produces head and eye movements in directions correlated with the position in the MASP [27,28]. However, recent findings demonstrated that microstimulation in the OT of the barn owl also induces pupil dilation responses, independent of gaze movements [29*]. Moreover, low intensity microstimulation can prime the site of stimulation in the MASP so that the pupil dilation response to an auditory stimulus presented later from the corresponding direction is enhanced [29*]. Similar results have been shown recently in primates [67] and support the emerging hypothesis that the evolutionary role of the OT/SC is to select stimuli based on saliency for directing orienting movements, overt and covert attention and autonomic responses (reviewed in [68,69]).

Conclusions

Since its discovery, the owl’s map of auditory space has provided ground for investigating the basis of the neural code. With time, the idea of a map of sound direction has evolved into a dynamic perspective of coding over time, where context and auditory-scene statistics are represented. This highly specialized creature, whose survival depends on sound localization, thus allows us to approach three of the most important questions in neuroscience: how information is represented, learned and categorized in the brain.

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