

Visual instruction of the auditory space map in the midbrain

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Introduction

Visual and auditory information about the location of objects is processed and combined in a midbrain nucleus called the optic tectum (also called the superior colliculus in mammals). A primary function of the optic tectum is to create a multimodal map of space that can be used to orient attention and gaze toward interesting stimuli, regardless of the source of the sensory information (Peck, 1996, Stein and Meredith, 1993).

The optic tectum receives spatial information from the visual and auditory systems that is mutually independent and complementary. Vision provides high resolution spatial information about the location of distant objects, even though they may be silent. Hearing provides spatial information about objects, even though they may not be visible. When objects can be both seen and heard, the cooperative combination of visual and auditory signals increases the capacity of the optic tectum to detect and locate stimuli under a wide range of difficult conditions (Stein and Meredith, 1993).

Combining spatial information across sensory modalities presents a challenging task to the nervous system, because visual and auditory information is initially encoded in completely different coordinate frames. Visual space is derived from the locus of activity within the topographic projections from the retina. In contrast, auditory space is derived from the evaluation of a variety of localization cues that arise from the interaction of incoming sound with the physical properties of the head and ears (Middlebrooks and Green, 1991). Auditory localization cues consist of interaural time differences (ITDs), which result from a difference in the distance traveled by a sound to reach the left versus the right ear, and interaural level differences (ILDs) and monaural spectral cues, both of which arise from the frequency-dependent directional properties of the external ears.

Visual and auditory spatial information is combined in the optic tectum by translating auditory cues into a topographic representation of space (Knudsen, 1982). The auditory system transforms its representations of cue values into a map of space by integrating information across frequency channels and across cues. This integration helps to resolve spatial ambiguities that are inherent to individual, frequency-specific cues and creates neurons that are broadly tuned for frequency, but sharply tuned for space (Brainard et al., 1992). The auditory map is aligned with the visual map of space in the optic tectum so that tectal neurons respond to either visual or auditory stimuli located in the same region of space (figure 1).

The mutual alignment of visual and auditory receptive fields in the tectum indicates that tectal neurons are tuned to the values of auditory cues that are produced by a sound source at the location of their visual receptive fields. Establishing and maintaining tuning to the correct values of auditory cues is made complicated by the variation in the correspondence between cue values and locations in the visual field that occurs across sound frequencies, across individuals, and within individuals during growth. Furthermore, the correspondence between encoded cue values and locations in the visual field changes with changes in the relative sensitivities of the ears and with development and aging of the nervous system. It is not surprising, therefore, that the tuning of tectal neurons to auditory localization cues is shaped by experience (Knudsen et al., 1984; King et al., 1988; Knudsen and Knudsen, 1989).

This chapter discusses how visual experience shapes auditory tuning in the optic tectum. We focus on data from the barn owl because its auditory map exhibits the highest resolution among all species studied and our knowledge of the effects of experience on

the map is most complete for this species. We describe mechanisms of adaptive auditory plasticity and the teaching signals that guide the plasticity. Finally, we present a model that accounts for the plasticity in terms of cellular mechanisms and principles of learning that are likely to apply equally well to other species and to other networks in the brain.

Innate Aspects of the Auditory Space Map

Many animals, including humans, can orient in the general direction of an auditory stimulus soon after birth (Ashmead et al., 1986, Morriongiello et al., 1994). This indicates that certain expectations about the relations between auditory localization cues and locations in space are preprogrammed into the auditory system. For this to happen, the relations must be constant and reliable across evolutionary time. What might those expectations be?

The fact that ears are located on either side of the head leads to a number of predictable relations between binaural cues and locations in space. First, simultaneous sound at the two ears corresponds to a stimulus located near the midline (0° azimuth). Second, left ear leading ITDs indicate stimuli to the left, and right ear leading ITDs indicate stimuli to the right, with the maximum ITD value indicating stimuli directly to each side. Third, ITD changes approximately (although not perfectly) as a linear function of azimuth. Analogous predictable relations hold for ILD cues. However, because the spatial patterns of ILD cues are more complicated and more frequency dependent than those of ITD cues and because they are affected greatly by the position and movement of the external ears, these relations are far less precise. Nevertheless, a map of auditory

space, particularly of the horizontal dimension, could be preprogrammed in the auditory system on the basis of these expectations.

Consistent with these predictable aspects of cue-location relations and the ability of animals to identify the general locations of sound sources soon after birth, the auditory space maps in young guinea-pigs, ferrets and barn owls that are raised with both eyelids suture from birth have a number of normal features: the map of azimuth is approximately normal, with frontal space represented at the rostral end of each tectum and progressively more contralateral locations represented progressively more caudal in the tectum (Knudsen et al., 1991, Withington, 1992 and King and Carlile, 1993). The influence of innate patterns of connectivity, that anticipate normal relation between auditory cues (especially ITD) and locations in space, are evident in the anatomical and functional effects of abnormal experience on the development of the auditory space map, discussed below.

Visual Calibration of the Auditory Space Map

Although auditory maps of space develop in the optic tecta of blind reared animals, the maps are not entirely normal: in guinea pigs, azimuthal tuning is abnormally broad (Withington, 1992); in ferrets, some units exhibit multiple receptive fields (King and Carlile, 1993); in owls, elevational tuning is often highly abnormal (Knudsen et al., 1991); and, in all species, there is a decrease in the precision of alignment between auditory and visual receptive fields. These data imply that vision helps to shape the development of the auditory space map. This implication is reinforced by the topography of the auditory space map in normal owls. The auditory space map over-represents

frontal space relative to peripheral space in a manner that is not predicted by the spatial patterns of auditory localization cues (Knudsen, 1982). Instead, the over-representation of frontal space mimics the expansion of frontal space that exists in the visual space map which, in turn, reflects the increased density of photoreceptors in the area centralis of the retina.

The shaping influence of vision on the development of the auditory space map has been demonstrated directly by raising owls with prismatic spectacles that displace the visual field horizontally (figure 2A and B). Barn owls cannot move their eyes by more than a few degrees from their resting positions. Therefore, prisms produce a chronic discrepancy between visual and auditory spatial information. The immediate effect of prisms is an optical displacement of visual receptive fields in the tectum. Sustained experience with the prism spectacles, over a period of 6 - 8 weeks, leads to a horizontal shift in auditory spatial tuning in the optic tectum that re-aligns auditory receptive fields with the optically displaced visual receptive fields (Knudsen and Brainard 1991). The basis for the horizontal shift of auditory spatial tuning is a shift in unit tuning to ITD, the dominant localization cue for azimuth (figure 2C). The adjustment of auditory tuning in response to prism experience is adaptive because it realigns the auditory and visual maps in the tectum and it adjusts the auditory orienting responses mediated by the tectum so that the animal foveates an auditory target viewed through the prisms. Analogous results have been reported for young ferrets that have had one eye removed and the other eye chronically deviated: Over time, auditory receptive fields in the optic tectum shift according to the deviation of the remaining eye (King et al., 1988). These experiments

demonstrate that visual signals, when available, are the dominate source of instructive information for shaping the auditory space map.

Site of Plasticity

The owl's auditory system processes sound localization cues in parallel in the midbrain and forebrain (Cohen and Knudsen, 1999). The midbrain pathway (figure 3) branches from the main tonotopic pathway at the level of the central nucleus of the inferior colliculus (ICC). In the ICC, auditory cue values are represented in frequency-specific channels (Wagner at al., 1987). The next structure in the pathway is the external nucleus of the inferior colliculus (ICX). Here, information about cue values is integrated across frequency channels to create neurons that are sharply tuned for space and are organized to form a map of space (Knudsen, 1983). This auditory space map is then conveyed to the optic tectum by a topographic projection (Knudsen and Knudsen, 1983).

A major site of adaptive plasticity is the ICX, where the map is created. In prism-reared owls that acquire a shifted map of ITD in the optic tectum, the map of ITD in the ICX is shifted as well. In contrast, the representation of ITD at the next earlier stage, in the ICC, remains normal (Brainard and Knudsen, 1993).

Associated with the adaptive shift of the ITD map in the ICX, there is a corresponding change in the anatomy of the axonal projection from the ICC to the ICX (figure 3B). The ICC-ICX projection in normal owls is topographic. In prism-reared owls that have acquired a shifted map of ITD in the ICX, the ICC-ICX projection is asymmetrically broader than normal with bouton-laden axons appearing at abnormal locations in the ICX where they could support the newly learned responses to abnormal

values of ITD (DeBello et al., 2001). Interestingly, the normal anatomical projection is also maintained in these owls, even though responses to the normal input are not expressed. Thus, both learned and normal circuitry can coexist in the ICX.

Pharmacological experiments in prism-reared owls also demonstrate that the ICX is a site of plasticity. Excitatory transmission in the ICX is glutamatergic and relies heavily on NMDA receptor currents (Feldman and Knudsen, 1994). Blocking selectively NMDA-receptors in the ICX by focal application of the NMDA receptor blocker, AP5, causes a reduction of about 50% of the normal auditory response. However, in owls that have been exposed to prisms, newly learned responses are far more sensitive NMDA receptor blockade (Feldman et al., 1996). These data indicate that newly functional synapses in the ICX, supporting learned responses, are richer in NMDA-receptors.

The instructive signal

Supervised learning

The adaptive plasticity of the auditory space map is an example of supervised learning. In supervised learning, one system or network serves as the instructor for another. The instructive signal carries information needed for learning and passes it on to a different network where it guides appropriate changes in the pattern of connectivity (Knudsen, 1994). In the midbrain auditory localization pathway, information from the visual system, which is the most reliable source for determining target location, guides the association of auditory cue values with the locations in the visual field that produced them. But what is the nature of this instructive signal, how does it reach the auditory system and how does it work?

The instructive signal could be generated in two different ways. It could be derived from a visual assessment of the accuracy of auditory orienting responses. The results of this evaluation could destabilize the auditory network when the stimulus is not successfully foveated, or reinforce the auditory network when the stimulus is acquired by the fovea. We refer to such a non-topographic signal as a foveation-based signal.

Alternatively, a topographic representation of visual space could provide a template for learning. In this case, patterns of auditory activity are compared with the visually-based template. Auditory inputs that contribute to a pattern of activity that matches the template are strengthened; those that do not are weakened. This type of signal is referred to as template-based signal.

Partial occlusion of the visual field

A template-based instructive signal and a foveation-based instructive signal lead to very different predictions about the adjustments in the auditory space map that would occur when distinct portions of the visual field are altered differently. In the case of a template-based signal, the adjustments that occur in the auditory space map depend on the visual conditions that exist in each corresponding portion of visual space. Therefore, elimination or alteration of visual input from a specific region of the visual field should only affect adjustments in the corresponding portion of the auditory space map. In contrast, in the case of a foveation-based signal, where adjustments are based on the accuracy of auditory orienting responses as evaluated by the center of gaze, all portions of the auditory map should adjust according to the visual conditions at the center of gaze.

Such an experiment was conducted recently by Hyde and Knudsen (2001A). Barn owls wore spectacles that blocked peripheral vision on one side. Since the eyes of owls are essentially immobile in the orbits, this manipulation established different visual conditions in the blocked periphery versus the unblocked center of gaze. These owls were then presented with a prolonged auditory-visual misalignment in the unblocked center of gaze either by optically displacing the visual field or by removing prisms from owls that had already acquired a shifted map of ITD. After several weeks of experience, the auditory space map in the tectum was examined to determine whether the auditory representation of the center of gaze and of the periphery were altered differently or whether the entire map was altered as predicted by the visual conditions at the center of gaze.

The results of this experiment are consistent with the hypothesis that the instructive signal is a template-based signal. Occlusion of the visual periphery reduced the adaptive change that occurred in the portion of the auditory space map representing the occluded part of the visual field (figure 4A). Conversely, occlusion of the center of gaze reduced the adaptive changes in the part of the auditory space map representing the center of gaze, but not in the part representing the periphery (figure 4B). The results demonstrate that a template-based instructive signal, coming from the visual system, is involved in the auditory learning process.

The source of the instructive signal to the ICX

Since the ICX is a site of plasticity, the instructive signal must enter and act in the ICX, but where does the signal come from? To identify possible sources of instructive

input, retrograde tracers were injected into the ICX. As a result, cell bodies in the optic tectum were labeled (figure 5, Hyde and Knudsen, 2000), indicating that neurons in the optic tectum project to the ICX. Because the primary target of ICX output is the optic tectum, this projection from the optic tectum to the ICX is referred to as a feedback projection.

The optic tectum receives visual spatial information both from the retina and the forebrain (Bravo and Pettigrew, 1981), and therefore is an excellent candidate source of a visual instructive signal to the ICX. Analysis of the locations of labeled somata following injections of tracer into the ICX shows that the distribution of labeled cells in the optic tectum changes systematically with the location of the injection site in ICX (figure 5B), demonstrating that the optic tectum-ICX feedback connection is topographically organized. Moreover, the point-to-point topography of the optic tectum-ICX projection mirrors that of the feed-forward auditory projection from the ICX to the optic tectum: Injections of tracers into the ICX result in anterogradely labeled axons and retrogradely labeled somata at the same location in the optic tectum. Most of the tectal cells that project to the ICX are located in an intermediate layer (figure 5C), and have dendrites that project radially into both the superficial layers, which receive direct input from the retina, and the deep layers, which receive auditory input from the ICX as well as visual input from the forebrain. Therefore, the morphology and location of the feedback cells puts them in a position to integrate visual and auditory information from a restricted region of space. This topographically organized input to the ICX is ideally suited to provide a spatial template for instructing changes in the auditory space map in the ICX.

Strong evidence for a topographic instructive signal originating in the optic tectum comes from lesion experiments (Hyde and Knudsen, 2001B). In these experiments, a restricted lesion was made unilaterally in the rostral part of the optic tectum (representing frontal space, figure 6A). Lesions were made in owls that had worn prisms for many weeks and that had acquired shifted auditory maps of space in the optic tectum. After the lesion was made, the prisms were removed, exposing the owls to normal optical conditions. The effect of the lesion on auditory map plasticity was tested in a frontal part of the map on both sides of the brain and, in addition, in a more peripheral part of the map on the lesioned side. Adaptive plasticity was eliminated specifically in the portion of the map that corresponded to the lesion, i.e., in the frontal part of the map on the lesioned side (figure 6B). Map adjustments were normal on the intact side of the brain. In the peripheral part of the map on the lesioned side, adaptive adjustments in the auditory map continued to occur, although their magnitude decreased. The decreased magnitude of adjustments on this side of the brain could be due to interference caused by the portion of the map that was rendered non-adjustable by the lesion. This interference could be mediated by lateral inhibition within the map (Zheng and Knudsen, 1999).

Restricted lesions in the optic tectum have a strikingly similar effect to blocking part of the visual field, discussed previously: both manipulations result in the specific elimination of adaptive changes in the corresponding part of the auditory space map. The data demonstrate that a visually-based, topographic instructive signal from the optic tectum controls adaptive auditory plasticity in the ICX. Similarly in ferrets, a topographic visual signal from the superficial layers of the superior colliculus have been shown to be essential for the normal development of the auditory space map (King et al., 1998).

Gating of the instructive signal

For visual activity to provide instructive information to the auditory space map, a stimulus object must be both seen and heard and the corresponding visual and auditory signals must be treated as though they originate from the same source. Visual activity from objects that do not produce sounds is not useful for instructing the auditory map. Conversely, auditory information about objects that cannot be seen cannot be visually calibrated. Therefore, the instructive visual activity to the auditory space map should be gated. If it were not, then this activity would interfere with the normal processing of auditory information and might induce plasticity at inappropriate times, leading to maladaptive changes in the auditory network. The system is, therefore, challenged with the task of selecting those visual objects that produce sounds. Moreover the nervous system must decide that the visual and auditory signals represent the same stimulus object. A number of studies have shown that auditory and visual stimuli are associated on the basis of common temporal modulations of auditory and visual signals (Radeau and Bertelson, 1977; Hershey and Movellan, 2000), previous knowledge regarding the nature of the stimulus object (Thurlow and Jack, 1973) and possibly on attention (Driver and Spence, 1998). All these factors may influence the access of the instructive signal to the ICX.

Maintenance role of the instructive signal

The instructive signal plays a role, not only in guiding plasticity, but also in maintaining a shifted auditory map. In prisms reared owls that have a shifted map in the

ICX, a lesion of the feedback connection from the optic tectum causes a gradual shift of the adapted auditory map back towards normal, even though the owl continues to wear prisms (Hyde and Knudsen, 2001B). This gradual shift occurs only in the region of the auditory map that corresponds with the site of the lesion. This indicates that instructive input is required to hold the map in its shifted state. It has been noted previously that in an ICX that is expressing a shifted map of space, inputs that support the normal map remain functional but that action potential responses to the normal inputs are differentially suppressed by inhibition (Zheng and Knudsen, 1999). It is not surprising, therefore, that when a visually-based instructive signal is eliminated, the map has a tendency to shift back towards an intermediate state between the normal and the shifted maps.

A model of adaptive plasticity in the ICX

Initial map formation.

We hypothesize that an auditory map of space is formed initially by vision-independent mechanisms. This is evident from the presence of a normal auditory map early in development even when visual input is altered or disrupted. The initial map would reflect genetically determined connections that anticipate the predictable relations of auditory localization cues with locations in space (described above) and self-organizational processes that strengthen connections that are synchronously activated by natural sounds (Kempler et al., 2001). However, the auditory space map in the absence of normal visual input does not develop to align precisely with the visual space map in the optic tectum.

Nature and mechanisms of the instructive signal in the ICX

Precise alignment of the auditory map with the visual map is guided by a topographic instructive signal to the ICX, originating in the tectum. The type of information carried by the instructive signal is not known. Three possible signals are illustrated schematically in figure 7. One possible signal (figure 7A) is the result of a comparison between visual and auditory spatial information that takes place in the optic tectum. The result of this comparison is sent back to the ICX in a topographic manner to reinforce connections in the ICX that contribute to a correct alignment of the maps or to destabilize the auditory network when the match is not successful. A second possible signal (figure 7B) is an adjusted auditory template that results from adaptive auditory plasticity in the superficial layers of the optic tectum. This shifted auditory map is sent back to the ICX as an auditory template that instructs auditory plasticity. A third possible signal (figure 7C) is a topographic representation of the visual field that is sent to the ICX as a visual template for instructing auditory plasticity.

All of these instructive signals require a gate to avoid irrelevant visual activation in the auditory system (see discussion above). In the case of a comparison signal (figure 7A), the gate can be achieved by a smart mechanism of coincidence detection that allows activation only when visual and auditory activation are likely to rise from a common source. However, if the signal is an auditory or visual template (figures 7B and C), an external gating mechanism is required. The site of gating differs: in the case of an auditory template signal the gating must be at the level of the visual input to the site of

plasticity in the OT, whereas in the case of a visual template signal the gating can be either at the level of the visual input or at the level of the cells projecting to the ICX.

To determine which of the signals actually operates in this system, it is essential to record the instructive signal in the ICX. If the signal represents a comparison between auditory and visual signals, ICX units will respond differentially to the alignment of bimodal stimuli. If the signal is an altered auditory template, a delayed adjusted auditory response should appear in the ICX. If the signal is a visual template, ICX units will be activated by visual stimuli originating from a restricted receptive field that overlaps the normal auditory receptive field.

The activity of ICX units has been monitored for visual responses. None have been observed, nor has any modulation of auditory responses by visual stimuli been observed. This result might mean that the instructive signal is not visual but rather an adjusted auditory template (figure 7B). However, the auditory responses in the superficial layers of the OT have long delays, typically 15- 20msec, compared to the 6 - 8 msec delays typical of ICX units. If the optic tectum-ICX signal is auditory, the time-course of auditory responses in the ICX should display a biphasic pattern, representing feedforward activation and instructive feedback. Examination of post stimulus time histograms measured in the ICX do not provide any evidence for such a biphasic pattern.

A recent finding, however, strongly implicates a visual template signal in the ICX (Gutfreund et al., 2001). When bicuculline, a GABA_A antagonist, is focally applied in the optic tectum, ICX units representing the equivalent location in space begin responding to visual stimuli (figure 8A). Moreover, the visual responses in the ICX have restricted receptive fields that match the auditory receptive fields expressed at the same site (figure

8B). Thus the optic tectum can, under certain conditions, send a visual template signal to the ICX. Such a template could instruct the adjustment of the auditory space map.

Normally the visual signals in the ICX are gated off by GABAergic inhibition in the tectum. It is assumed that under natural conditions, when the animal is interacting with the environment, only visual signals that are associated with auditory signals are permitted to enter the ICX to instruct adjustments in the auditory map.

Alignment of the auditory and visual maps

Assuming that the instructive signal is a visual template, auditory map plasticity could be achieved by mechanisms of Hebbian long-term potentiation (LTP) and long-term depression (LTD) (Brown et al., 1988; Mulkei and Malenka, 1992). A single ICX cell receives multiple inputs from the ICC representing a range of values for each cue. When instructive activity enters the ICX, active auditory inputs that synapse on neurons that are activated by the instructive signal are strengthened by LTP, and active auditory inputs that synapse on neurons not activated by the instructive input are weakened by LTD. Axonal remodeling and synaptogenesis may take place to increase the strength of the connections. Such a mechanism ensures that the ICC-ICX projections form an auditory map that matches the topography of the instructive signal.

The instructing synapse must be stable, unaffected by auditory activity. There is no evidence yet that the optic tectum-ICX projection is unaffected by auditory experience, however, it is known that this projection appears early in development, before hatching (Luksch et al., 2000), suggesting that no experience is required for the development of the optic tectum-ICX projection.

Timing problem

The mechanisms of learning suggested above (LTP and LTD) are based on correlated activity of pre and post synaptic neurons (Stent, 1973). Such mechanisms are suited to support self-organizational plasticity where different inputs compete for control over the activity of the post synaptic neuron. In supervised learning, however, synapses are selected based on the action of an instructive signal that may arrive long after the synapses that are to be modified are active. This is especially apparent in cases of motor learning. For example in learning goal directed movements (Georgopoulos, 1986), movement errors are fed back to the sensorimotor network long after the information is transmitted through the network. For correct adjustments to take place, some trace of the pattern of activation must persist in the network until the instructive signal arrives.

A similar timing problem occurs in the auditory localization system. Visual responses recorded in the ICX appear ~70 msec after the onset of a light stimulus (figure 8). In contrast, ICX units are activated by an auditory stimulus just 6-8 msec after sound reaches the ear. This implies that by the time a visual instructive signal associated with a short bimodal stimulus activates ICX units, they may have finished processing the auditory stimulus. Whatever learning mechanism is used, it must be able to accommodate such long delays. Moreover, the relative timing of auditory and visual signals in the ICX depends strongly on the distance of the bimodal stimulus from the animal. Due to the time it takes for sound waves to reach the ears, the delay between auditory and visual activity reaching the ICX decreases with the distance of the object out to about 20 meters, at which point, auditory and visual signals arrive simultaneously in the ICX. It is

assumed, therefore, that the precise timing of auditory and visual inputs to the ICX is not critical, but rather that auditory synapses can be influenced by an instructive visual activity arriving over a window of time of up to 60 msec following the arrival of auditory activation.

Conclusion

The optic tectum is a structure in the brain in which spatial information from visual and auditory modalities converges into a premotor network that controls gaze direction. In the optic tectum, the auditory and visual modalities form maps of space that are mutually aligned. To achieve alignment, spatial information in the auditory system, which is encoded initially by auditory localization cues such as ILD and ITD, is transformed into a topographic map of space. This transformation is shaped by experience. A major component of the experience dependent plasticity occurs in the ICX, the nucleus preceding the optic tectum in the midbrain auditory localization pathway. Auditory receptive fields are synthesized and a map of space is formed in the ICX. The representation of auditory cue values in the auditory maps of space in the ICX and optic tectum is shaped by visual experience.

We are beginning to understand how the visual system instructs auditory map plasticity in the ICX. The instructive signal that controls plasticity is organized topographically: visual-auditory experience in a certain region of space instructs plasticity in the corresponding region of the auditory space map. The source of this signal is the optic tectum, which receives visual information both from the retina and the forebrain. Connections from the optic tectum to the ICX are organized topographically.

This anatomical pathway is ideally suited to provide a visually-based template to the ICX.

When GABAergic inhibition is blocked in the optic tectum, ICX units respond to visual stimuli. These visual responses have restricted receptive fields that match the auditory receptive fields expressed at the same site. Thus, under certain conditions, the optic tectum is capable of sending a topographic representation of the visual field into the ICX. This visual activity could serve as a template for guiding adjustments in the auditory space map. Moreover, the gating of visual activity to the ICX may be the mechanism by which the instructive signal is controlled to prevent interference with normal auditory processing and avoid changes in the network that are not adaptive.

Unanswered questions in this system include the following: (1) What are the synaptic mechanisms that underlie the instructed modifications of auditory inputs to the ICX? (2) What are the pathways that control the gating of visual signals into the ICX? (3) What are the natural conditions that open the gate and permit visual activity to enter the ICX?

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Figure legends

Figure 1. Auditory and visual maps in the optic tectum A) Auditory and visual receptive fields measured from a bimodal unit in the optic tectum are plotted on a globe of space. The coordinates are relative to the visual axes of the owl. The visual receptive field, indicated by the circled V, was mapped by moving a light bar across the visual field. Responses of the unit to sound bursts (100 msec noise burst at 20dB above threshold) as a function of azimuth and of elevation, are shown below and to the right, respectively. The shaded area represents the area from which the sound response was more than 50% of maximum (auditory best area). B) Lateral view of the left optic tectum. The contour lines indicate the locations of units with similar tuning. The approximate location of the recording site in A is indicated. Abbreviations: C, contralateral; d, dorsal; r, rostral. Adapted from Knudsen, 1982.

Figure 2. Effect of prism experience on the ITD tuning of tectal neurons. A) An owl wearing prismatic spectacles. B) The visual receptive field of a tectal unit recorded before and after mounting prisms that displace the visual field by 23° to the left ($L23^{\circ}$). The globe represents space relative to the visual axes of the owl. The contours, projected onto the globe, indicate the locations from which sound produces similar ITD values. The immediate effect of prisms is a shift of visual receptive fields (indicated by a circled V). C) The ITD tuning of tectal neurons before and after 8 weeks of experience with $L23^{\circ}$ prisms. Both units had visual receptive fields centered at 0° azimuth. Before prisms (black line), the unit is tuned to about $0\mu\text{sec}$ ITD. After 8 weeks of $L23^{\circ}$ prism experience

ITD tuning at this site was shifted to 50 μ sec right-ear leading (gray line). The arrows indicate the mid-point of the range of ITD values that elicited more than 50% of the maximum response (best ITD). D) Best ITDs plotted versus the azimuth of the visual receptive field for tectal units before prism experience (gray circles) and after 8 weeks of wearing L23⁰ prisms. The dashed line indicates the regression of the best ITDs on visual receptive field azimuth before prisms (normal). A systematic shift in the relation between best ITDs and visual receptive fields is apparent. Data are from Brainard and Knudsen, 1993.

Figure 3. Schematic representation of the midbrain auditory localization pathway. A) Auditory localization cues are initially synthesized in frequency specific channels. This information ascends to the central nucleus of the inferior colliculus (ICC). From the ICC auditory information proceeds to the ICX. In the projection from ICC to ICX information about cue values is combined to produce spatially restricted auditory receptive fields and a map of space. This map is projected to the optic tectum (OT) through the topographic ICX-optic tectum pathway. In the optic tectum the auditory map merges with a visual map of space. B) Prism experience induces an anatomical change in the ICC-ICX projection. An abnormal rostralward projection appears in one side and in the other side a caudalward projection. The normal projection remains intact.

Figure 4. The effect of partial occlusion of the visual field on auditory map plasticity. The circles on the left represent visual space relative to the owl's center of gaze. The optical conditions in each region of visual space are indicated. Black indicates a region of the

field from which light is occluded, white indicates a normal unaltered region and the vertical lines indicate a region displaced by prisms. A) Adaptation to normal vision at the center of gaze and occlusion of the left visual periphery. The panel on the right side depicts the shifts in ITD tuning from the predicted normal as a function of the visual receptive field azimuth. The open circles indicate the ITD shifts obtained after 7 weeks of prism experience. Following this experience, the owl was exposed to the conditions indicated by the circle on the left. Sites with visual receptive fields in the center of gaze adapted significantly better than sites with visual receptive fields in the occluded periphery. Shaded box indicates the occluded region of visual space. B) Adaptation to occlusion of the center of gaze and prismatic displacement of the periphery. The panel on the right side depicts the shifts in ITD tuning from the predicted normal as a function of the visual receptive field azimuth. The open circles indicate the ITD shifts measured before the owl was exposed to the conditions indicated by the circle on the left. After experience with these conditions (gray circles), sites with visual receptive fields in the periphery adapted significantly better than sites with visual receptive fields in the occluded center of gaze. The shaded box indicates the occluded region of visual space and the hatched box indicates the region displaced by prisms. Data are from Hyde and Knudsen, 2001.

Figure 5. Topography of the optic tectum-ICX projection. A) Photomicrograph of a horizontal section through the tectal lobe. Injections of biotinylated dextran amine (BDA) and Fluoro-Gold (FG) were placed in the ICX. Arrows indicate injection sites. The FG injection was more caudal than the BDA injection. B) Composite camera lucida

reconstruction of the BDA and FG labelled cell bodies in the optic tectum resulting from the injections shown in A. Black circles indicate the locations of cell bodies labeled with BDA and gray circles indicate the locations of FG-labeled cell bodies. C) High magnification view of a transverse section through the optic tectum. Retrogradely labeled cells, located in layers 10 and 11, are indicated by arrowheads. Scale bars in A=500 μ m in B=250 μ m. Data are from Hyde and Knudsen, 2000.

Figure 6. The effect of a restricted lesion in the optic tectum on auditory map plasticity. A) Schematic representation of the left and right tectal lobes. The lesioned area in the rostral left tectum is indicated by the black region. The sites of recording, in the deep layers on both the lesioned and intact sides, are indicated. B) Normalized ITD tuning curves measured before (top) and after (bottom) removal of prisms. ITD values are given relative to the predicted normal best ITD. Vertical bars indicate the mean best ITD value relative to normal. Arrowheads indicate the normal ITD tuning. ITD curves measured on the lesioned side (left panels) maintained shifted tuning and did not adapt following the removal of prisms. In contrast, on the intact side (right panels) ITD tuning shifted back to normal. Data are from Hyde and Knudsen, 2001.

Figure 7. Three possible models for the instructed plasticity in the ICX. The circles on the left represent neurons in the ICX. The circles on the right represent neurons in optic tectum. A black arrowhead indicates a plastic connection. An empty triangle indicates a connection that is non-plastic during auditory-visual interactions. An ICX neuron receives inputs from various ITD channels (arrows from left). The correct value is

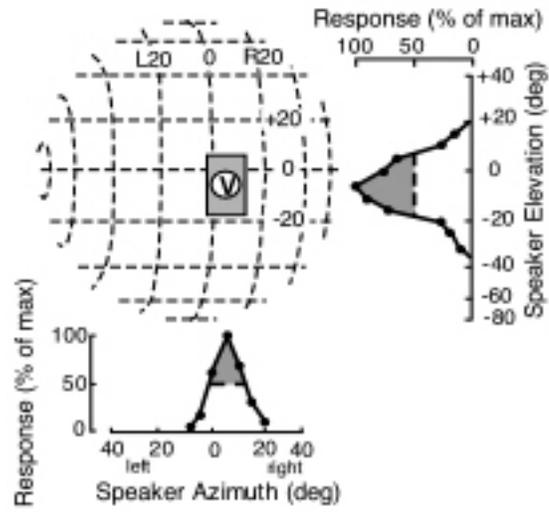
selected by a reinforcing instructive signal originating in the tectum (right circle). The different models assume different types of instructive signals. In A, the comparison model, the instructive signal is generated by cells in the tectum that compare auditory spatial information coming from the ICX with visual spatial information. If the spatial information from the two modalities is matched, the cell is activated and a signal is sent back to the optic tectum. In B, the auditory template model, the instructive signal is activated by a specific ITD value for each site. The selection of an ITD value is achieved in the superficial layers of the optic tectum by selecting auditory inputs from the deep layers of the tectum that carry ITD values that match a restricted visual input. In C, the visual template model, the instructive signal is activated by visual stimuli from a restricted region in space. This visual signal reinforces auditory inputs in ICX that are simultaneously activated.

Figure 8. The effect of bicuculline iontophoresis in optic tectum on visual responses in the ICX. A) Light flashes (50msec long) were presented every 5 seconds. The multi unit spike response to each presentation is shown by the dots along the vertical axis. The gray area indicates the time during which iontophoretic application of bicuculline was maintained. The horizontal line, at time 0, indicates the onset of light stimulus. In the ICX site (upper raster), units did not respond to light before iontophoresis of bicuculline. However, following six minutes of drug application in the optic tectum clear responses to light appear with a delay of about 70msec. In contrast, at the site of drug application (lower raster) light responses are measured before and during bicuculline iontophoresis. B) Light flashes or sound bursts of 50msec duration were presented from different

locations along the horizon (steps of 5° , each location 50 presentations). The post stimulus time histograms of multi unit recording are shown in black for the light stimulus and in gray for the sound stimulus (the auditory response is scaled by 0.5). Responses to light at this site were evident only when the LED was located 6° to the right of the owl's center of gaze. Strongest auditory responses were evoked when the speaker was located at the location that produced visual responses.

Figure 1

A Auditory and Visual Receptive Field



B Auditory Space Map in the Optic Tectum

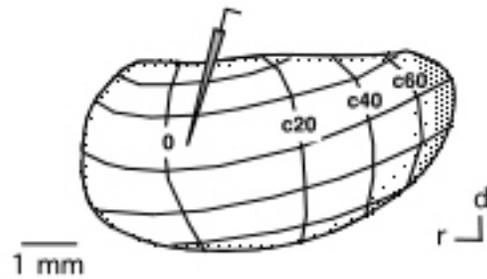


Figure 2

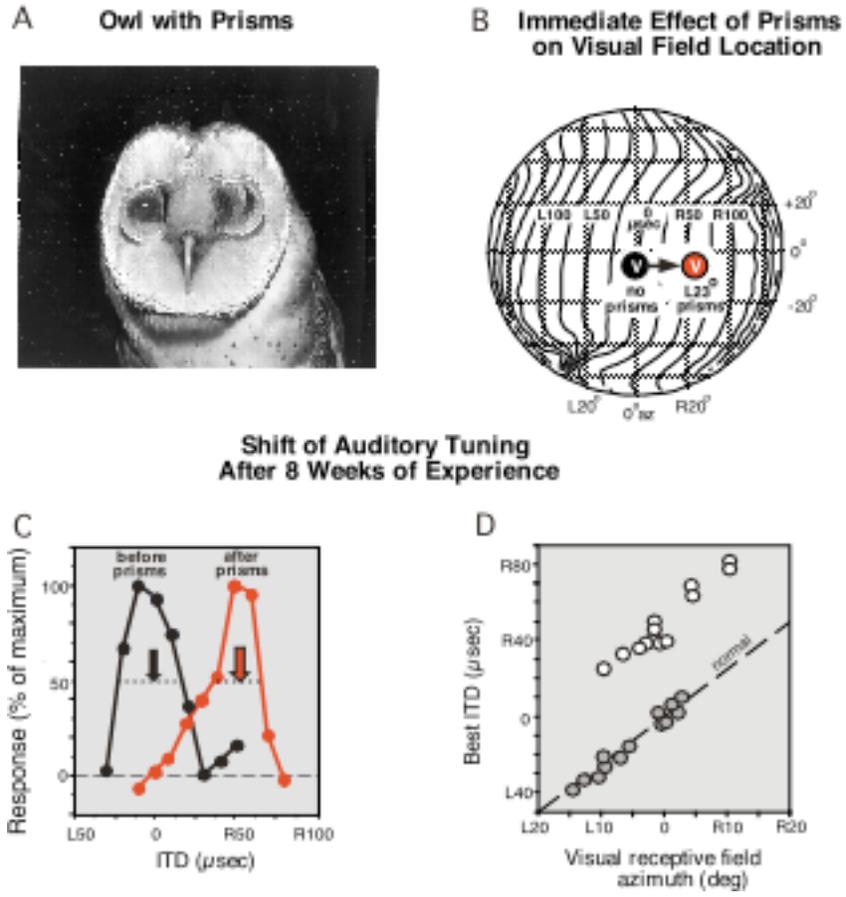


Figure 3

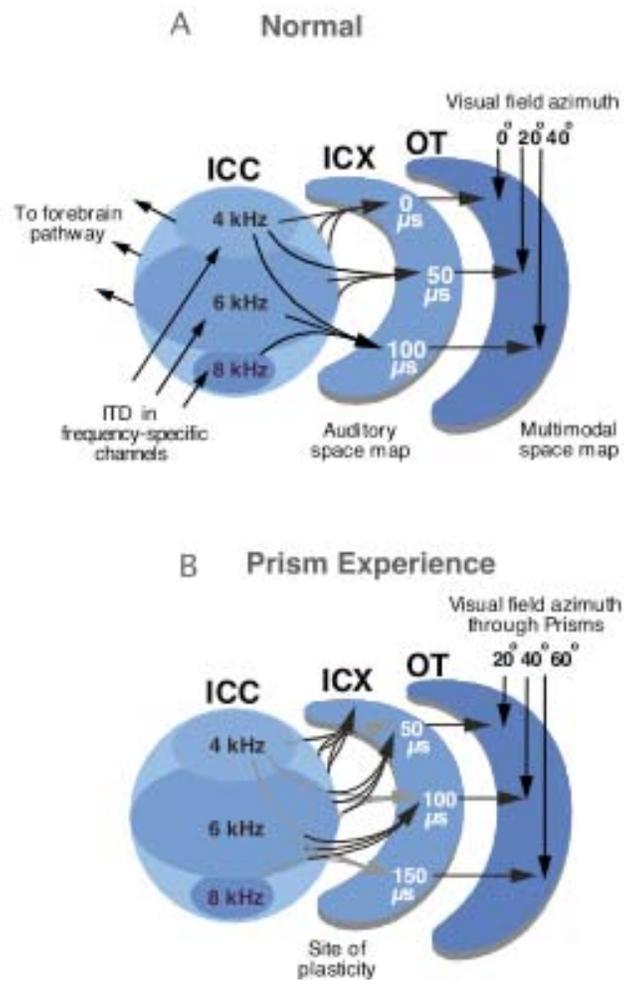


Figure 4

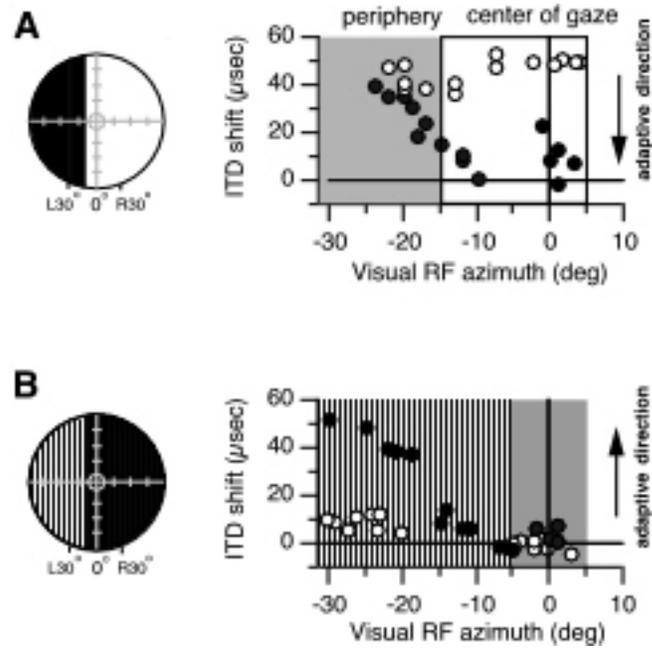


Figure 5

Topography of the optic tectum-ICX projection

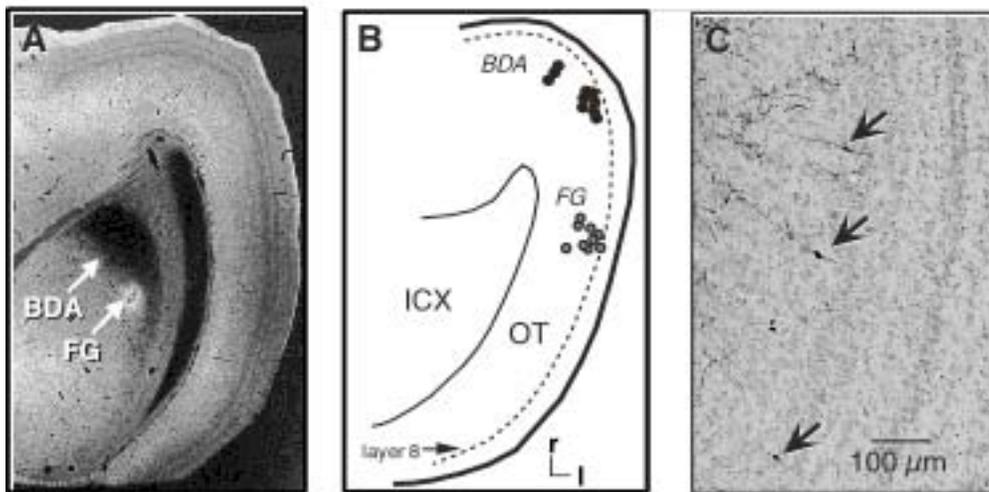


Figure 6

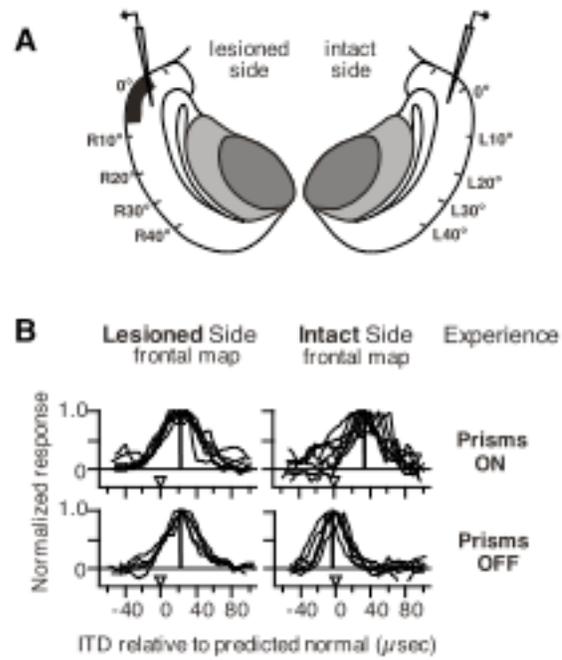


Figure 7

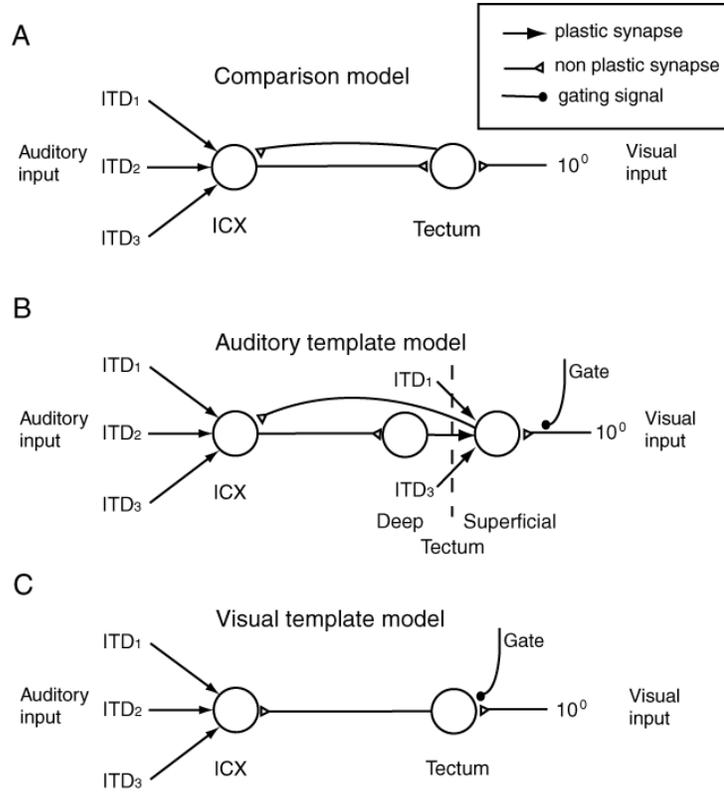


Figure 8

