Forebrain Pathway for Auditory Space Processing in the Barn Owl

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Cohen, Yale E., Greg L. Miller, and Eric I. Knudsen. Forebrain pathway for auditory space processing in the barn owl. J. Neurophysiol. 79: 891–902, 1998. The forebrain plays an important role in many aspects of sound localization behavior. Yet, the forebrain pathway that processes auditory spatial information is not known for any species. Using standard anatomic labeling techniques, we used a “top-down” approach to trace the flow of auditory spatial information from an output area of the forebrain sound localization pathway (the auditory archistriatum, AAr), back through the forebrain, and into the auditory midbrain. Previous work has demonstrated that AAr units are specialized for auditory space processing. The results presented here show that the AAr receives afferent input from Field L both directly and indirectly via the caudolateral projections of this area to midbrain and brain stem structures. Afferent input to Field L originates mainly in the auditory thalamus, nucleus ovoidalis, which, in turn, receives input from the central nucleus of the inferior colliculus. In addition, we confirmed previously reported projections of the AAr to the basal ganglia, the external nucleus of the inferior colliculus (ICX), the deep layers of the optic tectum, and various brain stem nuclei. A series of inactivation experiments demonstrated that the sharp tuning of AAr sites for binaural spatial cues depends on Field L input but not on input from the auditory space map in the midbrain ICX. Pharmacological inactivation of Field L eliminated completely auditory responses in the AAr, whereas bilateral ablation of the midbrain ICX had no appreciable effect on AAr responses. We conclude, therefore, that the forebrain sound localization pathway can process auditory spatial information independently of the midbrain localization pathway.

INTRODUCTION

The forebrain plays an important role in many different aspects of sound localization behavior (cf. Brainard 1994; Heffner and Heffner 1990; Heffner and Masterton 1975; Jenkins and Merzenich 1984; Knudsen and Knudsen 1996a,b; Ravizza and Diamond 1974). In particular, the auditory forebrain is involved critically in cognitive and complex spatiomotor tasks such as movements toward remembered auditory stimuli (Brainard 1994; Knudsen and Knudsen 1996b). Yet, the forebrain pathway for processing auditory space is unknown for any species.

In contrast, the midbrain sound localization pathway has been well described in both birds and mammals (cf. Knudsen 1984; Konishi et al. 1988; Stein and Meredith 1993). Moreover, the manner in which auditory spatial information is represented in this pathway also has been well characterized (cf. Irvine 1986; Knudsen 1984). However, the contributions of this pathway to the information processing that occurs in the forebrain sound localization pathway are not known.

Recently, we have begun to explore how auditory spatial information is represented in the forebrain of the barn owl. We have found an area in the forebrain archistriatum, the “auditory archistriatum” (AAr), that is at the apex of the auditory forebrain sensorimotor hierarchy (see also Dubbel-dam 1993; Zeier and Karten 1971). Unlike areas in the classical ascending auditory pathway, the majority of AAr sites have spatially restricted auditory receptive fields (Cohen and Knudsen 1995). The AAr and the area surrounding it are also essential for auditory spatial memory and for mediating changes in gaze to, and guiding movements toward, remembered auditory stimuli (Knudsen and Knudsen 1996a,b). These behaviors are mediated, in part, by efferent projections of this area to midbrain and brain stem structures that are known to be involved in movement control (Knudsen et al. 1995).

In this study, we used a “top-down” approach to characterize the forebrain pathway for processing auditory space in the barn owl. We identified an output area of this pathway (the AAr) and then traced the sources of input to this area using standard anatomic techniques. In addition to identifying a forebrain pathway that supplies input to the AAr, we sought to determine whether the auditory spatial information represented by an AAr site is dependent on the processing that occurs in the midbrain auditory space processing pathway or whether this information is derived independently in the forebrain.

METHODS

A total of 11 barn owls (Tyto alba) were used in this study; 9 of these owls were used also in our examination of the functional organization of Field L (Cohen and Knudsen 1996, 1998).

General methods

PREPARATION. Barn owls were prepared for repeated experiments. Owls were anesthetized with halothane (1%) and nitrous oxide (O₂:NO₂ = 55:45) while a headpiece was cemented to the skull and a craniotomy was made over particular areas of the forebrain. After opening the cranium, chloramphenicol (0.5%) ointment and Gelfoam (Upjohn) were applied to the brain surface. The craniotomy then was sealed with dental acrylic, and the incisions were infused with lidocaine HCl. After the owl recovered from the anesthesia, it was returned to its home cage.

On the day of an experiment, the owl was anesthetized, as described above, wrapped in a leather harness, suspended in a prone position inside a sound-attenuated chamber, and secured to a stereotaxic device by its headpiece. The head was positioned using retinal landmarks (the eyes are essentially stationary in the head) so that the visual axes were in the horizontal plane. The dental acrylic was removed from the craniotomy, and the experiments were started. At the conclusion of an experiment, chloramphenicol ointment and gelfoam were reapplied to the brain, the craniotomy...
was sealed with dental acrylic, and a subcutaneous injection of 2.5% dextrose in a saline solution was administered. On recovery from anesthesia, the owl was returned to its home cage.

**AUDITORY STIMULI.** Auditory stimuli were generated as described previously (Cohen and Knudsen 1994–1996). Dichotic stimuli consisted of 50-ms noise (filtered digitally for a bandpass of 1.0–12.0 kHz; 0-ms rise/fall times) or 50-ms tone (5-ms rise/fall times) bursts. The acoustic stimuli were transduced by Knowles earphones (model 1914) that were coupled to damping assemblies (BF-1743). The frequency response of each earphone was flattened (±2 dB between 1.0 and 12.0 kHz) by compensatory adjustments in the computer-generated waveforms. The output of the earphones was linear to within 0.2 dB over a 45 dB range of input amplitudes. Frequency-specific differences in timing and level between the two earphones ranged ±3 µs and 2 dB, respectively.

**NEUROPHYSIOLOGICAL RECORDINGS.** A lacquer-coated tungsten electrode (1–2 MΩ at 1 kHz) was advanced into the forebrain with a microdrive while neural activity was monitored on an audio monitor and an oscilloscope. Structures in the forebrain were identified on the basis of their frequency and binaural tuning properties and their stereotaxic location (see Cohen and Knudsen 1994–1996, 1998; Proctor 1993).

Response profiles were generated by presenting series of binaural stimuli consisting either of noise bursts with random sequences of interaural time differences (ITDs) or interaural level differences (ILDs) or of tone bursts with random sequences of frequencies. For each response profile, ≥10 repetitions of stimuli were presented. The response to a dichotic stimulus was quantified by subtracting the number of spikes occurring 100 ms before stimulus onset (baseline activity) from the number of spikes evoked during the 100 ms after stimulus onset. When ITD response profiles were being obtained, ILD was held constant at the site’s best value. Similarly, when ILD response profiles were being obtained, ITD was held constant at the site’s best value. Frequency response profiles were obtained with both ITD and ILD held at their respective best values based on responses to noise burst stimuli. ITD and ILD response profiles were generated over the entire physiological range (ITD: 200 µs left-ear leading to 200 µs right-ear leading; ILD: 30 dB left-ear greater to 30 dB right-ear greater) (Brainard et al. 1992; Knudsen et al. 1991, 1994; Olsen et al. 1989) using the dichotic noise stimulus. A site’s “best ITD” was defined as the range of ITDs that elicited responses that were >50% of the maximum response. The “best ILD” and the “best frequency” of a site were calculated in an analogous manner.

**Anatomic pathway tracing**

**INJECTION OF ANTEROGRADE AND RETROGRADE TRACERS.** Normally sealed the implanted guide tube was removed, and the anatomic pathway tracing was started. Similarly, when ILD response profiles were being obtained, ITD was held constant at the site’s best value. Frequency response profiles were obtained with both ITD and ILD held at their respective best values based on responses to noise burst stimuli. ITD and ILD response profiles were generated over the entire physiological range (ITD: 200 µs left-ear leading to 200 µs right-ear leading; ILD: 30 dB left-ear greater to 30 dB right-ear greater) (Brainard et al. 1992; Knudsen et al. 1991, 1994; Olsen et al. 1989) using the dichotic noise stimulus. A site’s “best ITD” was defined as the range of ITDs that elicited responses that were >50% of the maximum response. The “best ILD” and the “best frequency” of a site were calculated in an analogous manner.

**Inactivation experiments**

**INACTIVATION OF FIELD L.** In two control owls, a chronic guide tube was used to deliver lidocaine HCl, a Na⁺-channel blocker (see Hille 1967; Taylor 1959; Weidmann 1955), to Field L. A full description of this method can be found in Knudsen et al. (1993). Briefly, before the experiment day, a guide tube (21-gauge stainless steel) was cemented permanently in Field L while the owl was anesthetized. The guide tube was positioned, based on electrophysiological response properties, in the ventral two-thirds of the rostral terminal fields, and retrogradely labeled cells were reconstructed with a camera lucida.

HISTOLOGY. Survival times ranged from 1 wk (BDA) to 1 mo (Fluoro-Gold and rhodamine-coupled latex beads). The owls first were anesthetized deeply with ketamine (0.7–1.0 ml) and diazepam (0.08–0.12 ml). Next, intraventricular injections of heparin (300 units) and pentobarbital sodium (30 mg/kg) were administered, and the owls were perfused transcardially with a wash solution of 0.6% lidocaine HCl in 0.1 M phosphate buffer (PO₄ buffer; pH 7.4) followed by a fixative solution of 5% sucrose and 4% paraformaldehyde in PO₄ buffer. The brains then were cryoprotected in a solution of 30% sucrose and 4% paraformaldehyde in PO₄ buffer, blocked in the plane parallel to the plane of the electrode penetrations (the transverse plane), and cut on a freezing microtome in 40-µm sections. These sections then were mounted on glass slides.

The BDA labeling was visualized using a diaminobenzidine (DAB) reaction. Sections were rinsed in PO₄ buffer and incubated for 60 min at room temperature in a solution of avidin-biotin-peroxidase complex (Elite kit, Vector Laboratories). Sections were rinsed sequentially in PO₄ buffer and tris(hydroxymethyl)aminomethane-imidazole buffer (Tris-imid; pH 7.2) and then developed for 20 min in 0.4% DAB in Tris-imid with 0.003% H₂O₂ (Veenman et al. 1992; D. E. Feldman, personal communication). The label was enhanced by a 1-min incubation in 50% DAB Enhancing Solution (Vector Laboratories). Sections containing the rhodamine-coupled latex beads or the Fluoro-Gold were mounted on glass slides and cleared. Alternate sections were stained with cresyl violet or with a myelin (modified Gallyas) stain.

Sections containing fluorescent tracers were viewed under a fluorescence microscope while sections containing BDA were examined with light- and dark-field optics. Injection sites, labeled fibers, terminal fields, and retrogradely labeled cells were reconstructed with a camera lucida.

Inactivation experiments
INACTIVATION OF THE EXTERNAL NUCLEUS OF THE INFERIOR COLLIculus (ICX). The ICX was ablated bilaterally in one barn owl. The ICX was differentiated from other regions of the inferior colliculus by its unique electrophysiological properties (Brainard and Knudsen 1993; Mogdans and Knudsen 1993; Moitessier and Konishi 1981). ICX units are tuned sharply for both ITD and ILD and broadly tuned for frequency (tuning width at half-maximum > 2.4 kHz). Unit sensitivity for ITD and ILD is organized into a topographic map: best ITDs change systematically along the rostrocaudal axis and best ILDs change systematically along the dorsoventral axis. Electrolytic lesions in the ICX were made by passing 100 µA of cathodal current for 30 s through a 0.4-MΩ stainless steel recording electrode at multiple (2–3) sites in each electrode penetration. In individual dorsoventral electrode penetrations, lesions were separated by 200–250 µm, while individual electrode penetrations were separated by 200–250 µm. Lesions were placed at sites representing between contralateral 75 and ipsilateral 15 µs ITD and between +8 and −6 dB ILD. This range of best ITDs and best ILDs corresponds to the range of values represented by the vast majority of AAr sites (Cohen and Knudsen 1995). A week after the ICX was lesioned bilaterally, a tungsten microelectrode was used to assess the sensitivity of AAr sites to ITD and ILD in a manner similar to that described above.

RESULTS

Anatomy

Table 1 summarizes the pattern of anterograde and retrograde labeling that we observed in the barn owl forebrain.

Afferent and efferent connections of the AAr

AFFERENT CONNECTIONS. AAr units were identified by their consistently sharp tuning for both ITD and ILD. The AAr

<p>| Table 1. Summary of retrograde and anterograde label observed in the barn owl forebrain and midbrain |</p>
<table>
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<th>Case</th>
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<th>Retrograde Label</th>
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<td>PA, ICC, ICX, OT</td>
<td>L1–L3, Ncl</td>
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<td>AAr</td>
<td>PA</td>
<td>L1–L3, Ncl</td>
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AAr, auditory archistriatum; D, nucleus Darkshewitsch; H, hyperstriatum; ICC, central nucleus of the external nucleus; ICX, external nucleus of the inferior colliculus; InC, interstitial nucleus of Cajal; L1–L3, dorsal, middle, and ventral zones, respectively, of field L; LPO, lobus parolfactorius; MRF, mesencephalic reticular formation; nOv, nucleus ovoidalis; Ncl, caudolateral neostriatum; OT, optic tectum; PA, paleostriatum augmentum; Ru, red nucleus; SL, septal nuclei. *Label was restricted, in general, to the ventromedial aspect of the hyperstriatum.

is located approximately halfway along the rostrocaudal extent of the archistriatum, at the level of the anterior commissure (Fig. 1A). The AAr appears to be a subdivision of the archistriatal gaze fields, an area known to be involved in auditory spatial behavior (Knudsen and Knudsen 1996a,b); the exact relationship between these two areas, however, is not known. In three animals in which iontophoretic injections of BDA were placed in the physiologically defined AAr, a large population of retrogradely labeled somata were found in the ipsilateral Field L (Figs. 1 and 2B). Figure 1 illustrates the results obtained from one such injection and is representative of the results from the other two injections.

In the caudal portion of Field L, retrogradely labeled cells were restricted largely to the lateral third of Field L (Fig. 1E). More rostrally, labeled cells could be found along most of the mediolateral extent of Field L (Fig. 1D); only the most-medial edge did not contain labeled cells. Dorsoventrally, retrogradely labeled somata were found primarily in the middle (thalamorecipient) zone and in the ventral zone of Field L (Figs. 1, D and E); these two zones are often called L2 and L3, respectively (cf. Bonke et al. 1979; Wild et al. 1993) (see LOCAL CONNECTIONS WITHIN FIELD L). In addition to the retrograde label found in Field L, retrogradely labeled somata were found in the ipsilateral, caudolateral neostriatum (Ncl; Fig. 1F).

EFFERENT CONNECTIONS. The efferent connections of the AAr were examined in three animals. In one case, the AAr was targeted physiologically (Fig. 1A) and, in the other two cases, it was targeted stereotaxically. In all three cases, strong terminal fiber labeling was found in the ipsilateral paleostriatum augmentum (Fig. 1A; the avian analogue of the mammalian corpus striatum) (see Reiner et al. 1984), the ICX (Fig. 1C), and bilaterally in the deep layers of the optic tectum (Fig. 1C), and midbrain tegmental premotor nuclei (Fig. 1B) such as the nucleus Darkshewitsch, the interstitial nucleus of Cajal, the red nucleus, and the mesencephalic reticular formation; a weak projection to the ipsilateral central nucleus of the external nucleus (ICC) also was found. In addition to these projections, in one owl, terminal fiber labeling was found in regions of the ipsilateral, rostral forebrain including the lobus parolfactorius, a forebrain region associated with memory consolidation (for a review, see Konishi 1989, 1994; Rose 1991; Scheich 1987), and midline septal nuclei.

Connections of Field L

Field L was found to be a major source of efferent input to the AAr (Fig. 1). Therefore, we examined the afferent and efferent connections of Field L, as well as its intrinsic connections.

AFFERENT CONNECTIONS OF FIELD L. Retrograde tracers (rhodamine beads and/or Fluoro-gold) were injected into Field L of two owls. These injections were made at various locations corresponding to different frequency representations in Field L (Fig. 3, C and D) (see Cohen and Knudsen 1996). In both cases, a large population of retrogradely labeled somata were found ipsilaterally in the auditory thalamic nucleus, nucleus ovoidalis (see further); Fig. 3A illustrates the pattern of labeling in the nucleus ovoidalis from one case.
FIG. 1. Anterograde and retrograde labeling in the forebrain after a biotinylated dextran amine (BDA) injection into the auditory archistriatum (AAr). Camera lucida drawings of transverse sections illustrate the injection site (A) and the axons and somata that were labeled as a result of the injection. Myelination patterns used to identify different areas of the avian forebrain and midbrain are shown in gray. Injection site, in A, is represented by the black area. —— labeled axons; ● labeled somata. Camera lucida drawings illustrated in C–F are composites from ≥2 camera lucida drawings. Inset: planes of section. D, dorsal; M, medial; PP, paleostriatum primitivum; PA, paleostriatum augmentum; AC anterior commissure; D, nucleus Darkshewitsch; InC, interstitial nucleus of Cajal; Ru, red nucleus; MRF, mesencephalic reicular formation; ICX, external nucleus of the inferior colliculus; OT, optic tectum; L1–L3, dorsal, middle, and ventral zones, respectively, of Field L; H, hyperstriatum; N, neostriatum; W, Wulst; A, archistriatum.

FIG. 2. Afferent and efferent connections of Field L. A: high-magnification, dark field photomicrograph of a transverse section showing anterograde label in L2 after an injection of BDA into the nucleus ovoidalis (nOv). B: high-magnification, dark field photomicrograph of a transverse section showing retrogradely labeled somata in L3 after an injection of BDA into the AAr.
In addition, retrograde label also was found in various regions of the ipsilateral, rostral forebrain (data not shown), including the lobe parolfactorius, the lateral and medial septal nuclei, and the hyperstriatum ventrale, and, in one of these owls, the AAr.

**Efferent connections of Field L.** The efferent connections of Field L were examined in two owls with BDA as the anterograde tracer. The results of the two injections were similar. Figures 4 and 5 illustrate the pattern of label that resulted from one of these injections. In this owl, the injection was centered on the lateral half of the high-frequency, rostral Field L and included the middle (L2) and ventral zones (L3) of Field L (Fig. 4B). We observed labeled fibers and terminal fields in a number of ipsilateral forebrain structures. In particular, we observed labeled axons and a dense terminal field of branching fibers with varicosities in the dorsal AAr (Figs. 4A and 5B). This anterograde label in the AAr corroborated our observation of retrogradely labeled cells in Field L after injections into the AAr (Fig. 1). In addition, labeled fibers and terminal fields were observed ipsilaterally in a region of the Ncl at the anterior-posterior level of Field L (Figs. 4C and 5C), in the lateral aspect of the paleostriatum augmentum (Fig. 4A), and in the rostral neostriatum at the anterior-posterior level of the paleostriatum augmentum (Fig. 4A). The projection from Field L to the Ncl might be analogous to the projection from Field L to the neostriatum dorsale that has been described in other avian species (cf. Bonke et al. 1979; Wild et al. 1993). The projection from Field L to the paleostriatum augmentum (Fig. 4A) and observing retrogradely labeled somata (Fig. 4B) has been described in other avian species (cf. Shimizu et al. 1995).

The projection from Field L to the paleostriatum augmentum was confirmed by injecting rhodamine beads into the paleostriatum augmentum (Fig. 6A) and observing retrogradely labeled somata in Field L (Fig. 6B).

**Local connections within Field L.** Based on histological reconstructions of electrophysiological recording sites, Field L is coextensive with three cytologically distinct regions of the caudal neostriatum (Fig. 7) (Cohen and Knudsen 1996). The “dorsal zone” of Field L overlaps with a comb-like band of fibers that is oriented approximately perpendicular to the horizontal plane. The “middle zone” overlaps with a neostriatal region that contains a dense plexus of fibers and small, densely packed somata and that stains heavily for cytochrome oxidase (data not shown). Based on its cytoarchitecture, myeloarchitecture, and staining for cytochrome oxidase, it would appear that this middle zone corresponds to the neostriatal region termed Field L by Rose (1914) (see also Bonke et al. 1979; Braun et al. 1985; Karten 1968; Wild et al. 1993). The “ventral zone” of Field L overlaps with a dense meshwork of fibers located ventrally in the middle zone (Field L of Rose). We will adopt a nomenclature that has been used in other avian species (cf. Bonke et al. 1979; Wild et al. 1993) and refer to the dorsal, the middle, and the ventral zones of Field L as L1, L2, and L3, respectively.

To investigate the local connections of Field L, small injections of Fluoro-gold or BDA were placed into L1 and L3 of three different owls. The results of these injections, summarized in Fig. 8, indicate that, like other birds (cf. Scheich 1990), the primary source of input to the L3 is from the L2 (Fig. 8A) whereas the L1 receives afferent input from both L2 and L3 (Fig. 8, B and C).

**Afferent and efferent connections of the nucleus ovoidalis**

The nucleus ovoidalis was found to be a major source of afferent input to Field L. Therefore, we examined the afferent and efferent connections of the nucleus ovoidalis with other portions of the forebrain and midbrain by iontophoresing BDA into the nucleus ovoidalis of two barn owls. The results of these injections were similar. Figure 9 illustrates the pattern of label that resulted from one injection. After an injection into the nucleus ovoidalis (Fig. 9A), we found retrogradely labeled somata in all regions of the ipsilateral ICC but not in the external nucleus of the inferior colliculus (Fig. 9B). Labeled fibers and terminal fields were found throughout the mediolateral extent of the ipsilateral L2 (Figs. 9B and 9C).
FIG. 5. Anterograde labeling in the barn owl forebrain resulting from an injection of BDA into L2. Injection site is shown in A. B and C: high-magnification, dark-field photomicrographs of transverse sections showing anterograde BDA labeling in (B) the AAr and (C) the caudolateral neostriatum (Ncl). Scale bars in B and C equal 200 μm. V, ventral.

2A and 9C), corroborating the retrograde label in the nucleus ovoidalis that resulted from injections into Field L (Fig. 3). We should note that, unlike other avian species (cf. Durand et al. 1992; Karten 1968; Wild et al. 1993), the barn owl auditory thalamus does not appear to contain any subdivisions (see also Proctor 1993).

Summary of connections

Figure 10 summarizes the major connections that we observed in the barn owl. We observed two pathways by which information from the ICC reaches the AAr. The first pathway, the “direct” pathway, is as follows: ICC → nucleus ovoidalis (nOv) → Field L → AAr. All three zones of Field L, but particularly L2 and L3, project to the AAr; L2 supplies a major input to L3. The second pathway, the “indirect pathway” is as follows: ICC → nOv → Field L → caudolateral neostriatum → AAr. AAr efferents terminate in the paleostriatum augmentum, the ICC, ICX, optic tectum, and brain stem premotor nuclei.

Inactivation experiments

This anatomic study revealed major pathways from the ICC to the AAr (see Fig. 10). The direct pathway is intriguing because neurons at each step of this pathway are sensitive to or tuned for binaural spatial cues (Cohen and Knudsen 1995, 1998; Konishi et al. 1988; Proctor 1993). However, we do not know whether the space-tuned neurons in the AAr are derived from information provided by Field L or, alternatively, from space-tuned responses in the ICX that are transmitted to the AAr via some unknown pathway. To distinguish between these possibilities, we investigated the effects of inactivating Field L or the ICX on the responses of AAr neurons to binaural spatial cues.

Inactivation of Field L

The hypothesis that Field L is the major source of input to the AAr (Fig. 10) was tested by inactivating Field L and examining AAr responsivity (see METHODS). This effect was examined at three AAr sites in two barn owls. The data shown in Fig. 11 illustrate a typical result. We quantified the effect shown in Fig. 11 by comparing the firing rate of the AAr site shown during a “control” period (4 min before lidocaine application in Field L), a “postinjection” period (7 min after drug application), and a “recovery” period (25 min after drug application). An analysis of variance indicated that the firing rate at this site varied significantly.
through the auditory midbrain. In the most medial penetrations, we found responses typical of the lateral shell of the central nucleus of the inferior colliculus (ICCLS) (see Wagner et al. 1987); sites were tuned for frequency, ILD, and interaural phase difference and were organized both tonotopically and according to their interaural phase difference tuning. In more lateral penetrations, which, based on stereotaxic coordinates, should have been in the ICX, we could not elicit any auditory-evoked unit activity. Further laterally, we encountered bursty units characteristic of the superficial layers of the optic tectum (see Knudsen 1982).

Histological reconstruction confirmed that ~90% of the ICX had degenerated or contained extensive gliosis (Fig. 12). Only the caudal 10% of the ICX, which contains sites that are tuned for ITD values not commonly found in the AAr (>100 μs contralateral-ear leading) (see Cohen and Knudsen 1995) remained. On the left side of the brain, there was additional damage and gliosis in the deep fiber tract that runs ventral to the ICX and that provides input to the optic tectum from both the ICX and the archistriatum (Knudsen and Knudsen 1983; Knudsen et al. 1995); on the right side, damage was confined to the ICX.

Despite the near-total bilateral ablation of the rostral ICX, auditory responses in the left and right AAr were robust. Typical ITD and ILD response profiles obtained from two AAr sites after bilateral ICX ablation are illustrated in Fig. 13. The selectivity of these sites for specific values of ITD or ILD did not differ appreciably from the selectivity of AAr sites in normal, nonlesioned owls (Cohen and Knudsen 1995).

**DISCUSSION**

This study describes a direct anatomic pathway that leads from the inferior colliculus to the AAr, an output area of the forebrain sound localization pathway (see Fig. 10). An indirect pathway, via the Ncl, also was identified. In addition, we have shown that the auditory responses of AAr units are dependent on input from Field L but not on input from the ICX (see Figs. 11 and 13). This observation indicates that the representation of auditory space in the forebrain is independent of the midbrain space processing pathway.

In the discussion that follows, we describe evidence that
suggests that the direct pathway from the ICC to the AAr is specialized for auditory space processing and that it plays a similar role in other birds. In addition, we compare this pathway with that seen in mammals, and we speculate as to why independent representations of auditory space are created in the forebrain and midbrain.

**Forebrain auditory space processing pathway**

Based on several lines of evidence, we believe that the direct pathway from the inferior colliculus to the AAr (see Fig. 10) is involved in auditory space processing. First, neurons in all of the sites of this pathway are sensitive to binaural spatial cues (see Cohen and Knudsen 1998; Konishi et al.)
FIG. 11. Effect of Field L inactivation on AAr responses. Peristimulus time histograms of auditory unit responses measured in an AAr site during 4 different time periods: 4 min before lidocaine injection and 7, 16, and 25 min postinjection. Each peristimulus time histogram represents responses to 20 auditory stimulus presentations. Gray bars indicate the duration (50 ms) of the auditory stimulus.

1988; Proctor 1993). Moreover, in the AAr, the highest processing level in this pathway, the majority of sites are not simply sensitive to binaural cues but, instead, are tuned for specific binaural cue values and have spatially restricted auditory receptive fields (Cohen and Knudsen 1995). Second, consistent with their electrophysiological properties, behavioral experiments have demonstrated that both the auditory thalamus and the area surrounding and including the AAr are involved in auditory orienting behavior (Knudsen and Knudsen 1996a; Knudsen et al. 1993). More recent work has shown that the area surrounding and including the AAr is also essential for auditory spatial memory (Knudsen and Knudsen 1996b). Finally, microstimulation in the area surrounding and including the AAr evokes saccadic head turns similar to those that occur naturally (Knudsen et al. 1995).

The pattern of connectivity seen in the direct pathway is reminiscent of that seen in other avian species (cf. Bonke et al. 1979; Brauth and McHale 1988; Brauth et al. 1987, 1994; Dubbeldam 1993; Karten 1968; Kelley and Nottebohm 1979; Vates et al. 1996; Wild et al. 1993). In all birds, auditory information from Field L projects directly and indirectly, via structures in the neostriatum, to the anterior archistriatum (the archistriatal region containing the barn owl AAr). Based on these similarities, we suggest that the pathway leading from Field L to the archistriatum plays a similar role in auditory space processing in other avian species (see also Dubbeldam 1993).

Comparison with mammalian species

A forebrain auditory space processing pathway has not been characterized fully in any mammal. However, based

FIG. 12. Transverse, myelin-stained sections through the inferior colliculus of a barn owl with bilateral lesions in the ICX: A is from the left inferior colliculus and B is from the right inferior colliculus. For comparison, a section through the inferior colliculus of a nonlesioned barn owl is shown in C. Inset: plane of section.
on many different anatomic studies, it is reasonable to believe that, in the primate, a forebrain auditory space processing pathway would be the following: auditory thalamus (the medial geniculate nucleus) → primary auditory cortex (AI) → PaAlt, PaAc → Tpt → frontal eye fields (FEF) (cf. Chavis and Pandya 1976; Clarey et al. 1992; Colombo et al. 1996; Jones and Powell 1970; Pandya 1995; Pandya and Sanides 1973; Pandya and Yeterian 1985; Petrides and Pandya 1984; Schall et al. 1995; Wegener 1973). The PaAlt and the PaAc are part of the nontonotopically organized “belt” region of the auditory cortex, whereas the Tpt is considered part of the auditory “association” cortex. The observation that units in the AI (cf. Middlebrooks and Petti- grew 1981; Middlebrooks et al. 1980; Rajan et al. 1990), Tpt (Leinonen et al. 1980), and the FEF (Russo and Bruce 1994; Vaadia et al. 1986) are sensitive to the spatial location of a sound source supports the notion that this proposed pathway is involved in spatial processing. However, it is important to note that our understanding of the representations of auditory space in the FEF and the Tpt is quite rudimentary, and the spatial tuning properties of the PaAlt and the PaAc are unknown. Moreover, it is unknown whether the representation of auditory space in the mammalian forebrain is created independently of the midbrain space processing pathway.

**Functional specialization of the forebrain auditory space processing pathway**

The role of the forebrain and midbrain auditory space processing pathways can be differentiated based on the nature of the task. More specifically, we propose that the forebrain pathway primarily participates in voluntary shifts of gaze, such as those that require access to memory stores, and that the midbrain pathway participates in all saccadic orienting movements to sounds and is particularly important for short latency, reflexive orienting movement. This division of function can be seen in behavioral studies in which various forebrain areas have been inactivated. For example, after ablation of the AAr and the area surrounding it or the auditory thalamus, barn owls can orient and fly toward auditory targets that are still present in the environment but cannot orient to a remembered target (Knudsen and Knudsen 1996a,b; Knudsen et al. 1993). Similarly, after ablation of the auditory cortex, mammals still can orient their gaze immediately toward auditory targets but cannot respond to a sound no longer present in the environment (cf. Heffner and Heffner 1990; Heffner and Masterton 1975; Jenkins and Merzenich 1984; Ravizza and Diamond 1974). A similar division of function between the forebrain and the midbrain grew 1981; Middlebrooks et al. 1980; Rajan et al. 1990), Tpt (Leinonen et al. 1980), and the FEF (Russo and Bruce 1994; Vaadia et al. 1986) are sensitive to the spatial location of a sound source supports the notion that this proposed pathway is involved in spatial processing. However, it is important to note that our understanding of the representations of auditory space in the FEF and the Tpt is quite rudimentary, and the spatial tuning properties of the PaAlt and the PaAc are unknown. Moreover, it is unknown whether the representation of auditory space in the mammalian forebrain is created independently of the midbrain space processing pathway.

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FOREBRAIN AUDITORY SPACE PROCESSING PATHWAY


