Early Auditory Experience Induces Frequency-Specific, Adaptive Plasticity in the Forebrain Gaze Fields of the Barn Owl

GREG L. MILLER AND ERIC I. KNUDSEN
Department of Neurobiology, Stanford University School of Medicine, Stanford, California 94305

Received 24 October 2000; accepted in final form 16 January 2001

Miller, Greg L. and Eric I. Knudsen. Early auditory experience induces frequency-specific, adaptive plasticity in the forebrain gaze fields of the barn owl. J Neurophysiol 85: 2184–2194, 2001. Binaural acoustic cues such as interaural time and level differences (ITDs and ILDs) are used by many species to determine the locations of sound sources. The relationship between cue values and locations in space is frequency dependent and varies from individual to individual. In the current study, we tested the capacity of neurons in the forebrain localization pathway of the barn owl to adjust their tuning for binaural cues in a frequency-dependent manner in response to auditory experience. Auditory experience was altered by raising young owls with a passive acoustic filtering device that caused frequency-dependent changes in ITD and ILD. Extracellular recordings were made in normal and device-reared owls to characterize frequency-specific ITD and ILD tuning in the auditory archistriatum (AAr), an output structure of the forebrain localization pathway. In device-reared owls, individual sites in the AAr exhibited highly abnormal, frequency-dependent variations in ITD tuning, and across the population of sampled sites, there were frequency-dependent shifts in the representation of ITD. These changes were in a direction that compensated for the acoustic effects of the device on ITD and therefore tended to restore a normal representation of auditory space. Although ILD tuning was degraded relative to normal at many sites in the AAr of device-reared owls, the representation of frequency-specific ILDs across the population of sampled sites was shifted in the adaptive direction. These results demonstrate that early auditory experience shapes the representation of binaural cues in the forebrain localization pathway in an adaptive, frequency-dependent manner.

INTRODUCTION

Certain aspects of the representation of auditory information in the forebrain are shaped by an animal’s experience. For example, the representation of frequency in the primary auditory cortex can be modified by behavioral training (Bakin and Weinberger 1999; Recanzone et al. 1993) or sensory deprivation (Rajan et al. 1993). Experience-dependent plasticity also shapes the forebrain representation of other types of auditory information, including high-order stimulus features that are not encoded at the level of the cochlea (Doupe and Solis 1997; Margoliash 1983; Volman 1993). In this study, we investigate the effects of auditory experience on the forebrain representation of binaural cues that are used for sound localization.

Accurate sound localization requires that the auditory system establishes associations between binaural localization cues, such as interaural time and level differences (ITDs and ILDs), and the locations in space that produce them. These associations are established in parallel pathways in the midbrain and forebrain (Cohen and Knudsen 1999). In the midbrain localization pathway of the barn owl, experience early in life shapes the neural representation of binaural cues in an adaptive manner (Brainard and Knudsen 1993; Gold and Knudsen 2000a; Mogdans and Knudsen 1992). Much less is known about the influence of experience on the forebrain localization pathway.

An output structure of the forebrain localization pathway is the forebrain gaze fields, which contribute to voluntary changes in gaze (Knudsen and Knudsen 1996a). In mammals, this structure is the frontal eye fields and in birds, it is referred to as the archistriatal gaze fields (AGF) (Knudsen et al. 1995). In owls, the AGF plays an essential role in complex tasks, such as directing the owl’s gaze to the location of remembered auditory targets (Knudsen and Knudsen 1996b). The auditory subdivision of the AGF, the auditory archistriatum (AAr), contains units that have spatially restricted auditory receptive fields and are tuned to specific values of ITD and ILD (Cohen and Knudsen 1995). The tuning of AAr units for localization cues and the contribution of the AAr to orienting movements both persist following inactivation of the midbrain localization pathway (Cohen et al. 1998; Knudsen and Knudsen 1996a). Thus the forebrain pathway is capable of operating independently of the midbrain pathway.

One study has already demonstrated that the representation of auditory space in the AAr is shaped by experience (Miller and Knudsen 1998). In that study, young owls were raised wearing prismatic spectacles that caused a horizontal displacement of the visual field. In this study, we subjected owls to a different and more severe challenge. We used a passive acoustic device that altered the timing and level of sounds reaching the eardrum in a frequency-dependent manner (Gold and Knudsen 1999). The device changed the correspondences of ITD and ILD values with locations in space in different ways for different frequencies. To adapt to this manipulation, neurons in the localization pathway must be able to make frequency-specific changes in their ITD and ILD tuning. The results presented here demonstrate that neurons in the AAr are capable of this type of adaptive plasticity.
METHODS

Owls used in this study were cared for in accordance with the Stanford University Institutional Animal Care and Use Committee and the National Institutes of Health Guide for the Care and Use of Laboratory Animals.

Auditory experience

Monaural hearing impairment was imposed by raising owls with a monaural filtering device that caused frequency-dependent changes in ITDs and ILDs (Fig. 1). The filtering device was a lightweight plastic chamber (acetal delrin; Plastics SRT) that was sutured into the right ear canal of juvenile owls between the ages of 35 and 100 days. During implantation of the device, an owl was anesthetized with halothane (1.5%) in a mixture of oxygen and nitrous oxide (55:45). The owl was allowed to recover fully from the anesthetic before being returned to the aviary. The device was re-sutured periodically to maintain a tight fit. Owls wore the device for at least 60 days before any electrophysiological measurements were made.

Electrophysiology

Owls were prepared for multiple electrophysiological experiments. Prior to these experiments, an owl was anesthetized with halothane and nitrous oxide, and a headpiece was mounted to the skull. At the same time, a craniotomy was made over the optic tectum and AAr. Chloramphenicol antibiotic (0.5%) was applied to the exposed brain surface, and the craniotomies were sealed with dental acrylic. All wounds were infused with lidocaine hydrochloride (Xylocaine, 2%), and the owl was allowed to recover fully from anesthesia before being returned to the aviary.

On the day of an experiment, an owl was anesthetized with halothane and nitrous oxide. The acoustic device was removed, and the ear canals and ear canals were inspected for damage and cleaned of earwax. The owl was then wrapped in a leather harness, suspended in a prone position inside a sound-attenuating chamber (AD2000, Eckel Industries), and secured to a stereotoxic device by its headpiece. The head was positioned using retinal landmarks so that the visual axes were in the horizontal plane, and the dental acrylic was removed from the craniotomy. Light anesthesia was maintained throughout the experiment by periodic application of nitrous oxide alone or, occasionally, by application of both nitrous oxide and halothane.

Insulated tungsten microelectrodes (1–3 MΩ at 1.0 kHz) were positioned stereotaxically and advanced through the brain with a microdrive. A level discriminator was used to isolate a small number (1–3) of units; no attempt was made to ascertain whether a recording was exclusively from a single unit. The timing of action potentials elicited by auditory stimuli was stored on a computer. To calibrate the position of the electrode in the brain, the electrode was first advanced into the optic tectum. Since the visual map in the optic tectum is precise and well characterized (Knudsen 1982), the position of the electrode within the tectum can be determined from the location of the visual receptive field (VRF) of the recorded units. The AAr is located approximately 2.0 mm rostral, 0.5 mm lateral, and 3.0 mm dorsal to the representation of 0° azimuth and 0° elevation in the superficial layers of the optic tectum.

Throughout an experiment, chloramphenicol antibiotic was applied to the exposed brain surface. At the conclusion of an experiment, the craniotomy was resealed with dental acrylic, an intramuscular injection (2–3 ml) of 2.5% dextrose saline solution was administered, and the craniotomy. Light anesthesia was maintained throughout the experiment by periodic application of nitrous oxide alone or, occasionally, by application of both nitrous oxide and halothane.

Auditory measurements and assessment of binaural tuning

Auditory stimuli were generated digitally and delivered dichotically via earphones (Knowles earphones model 1914 coupled to damping assemblies BF-1743) placed in the external ear canals. Each earphone was aligned parallel to the long axis of the ear canal and centered within the canal approximately 5 mm from the tympanic membrane. The timing, level, and passband of sound presented at the two ears was under computer control.

Broadband and narrowband noise-burst stimuli (50-ms duration) were presented at an average binaural level (the sum of the sound level, in dB, presented at the 2 ears divided by 2) 20 dB above unit threshold. Broadband stimuli had a passband of 3–12 kHz and rise/fall times of 0 ms. Narrowband stimuli had 1- to 2-kHz bandwidth and rise/fall times of 5 ms. Narrowband stimuli with 1-kHz bandwidth were used preferentially, although at some sites it was necessary to increase the bandwidth to elicit reliable responses. At each site, ITD and ILD tuning was assessed separately using four different stimuli: broadband noise and narrowband noise centered on 4, 6, and 8 kHz, respectively. In some cases, however, units were lost before a complete set of measurements could be made.

A series of binaural stimuli consisted of noise bursts with ITD or ILD values presented in random order. For each tuning curve, at least 10 identical series of stimuli were presented. Net response to a noise burst was quantified by subtracting the number of spikes occurring during the 100-ms interval prior to stimulus presentation (baseline) from the number of spikes occurring during the 100 ms following stimulus onset. The range of ITD values that elicited at least 50% of

---

**FIG. 1.** The acoustic effects of the filtering device. The frequency-dependent effects of the device on the timing (A) and level (B) of sound reaching the eardrum of the ear fitted with the device, as measured with cochlear microphonics (Gold and Knudsen 1999). A: the thick black line indicates the median change in timing caused by the device in 5 owls for a sound located straight ahead, at 0° azimuth, 0° elevation; thin black lines indicate the range of timing changes across owls. B: the thick black line indicates the median change in level caused by the device in 6 owls for a sound located at 0° azimuth, 0° elevation; thin black lines indicate the range of level changes across owls.
the maximal response for a site was interpolated, and this range defined the site’s “ITD tuning width.” The left-ear leading end point of this range defined the site’s “left 50% cutoff,” and the right-ear leading end point defined the “right 50% cutoff.” The midpoint of this range defined the site’s “best ITD.” Tuning for ILD was determined and quantified in an analogous fashion. ITD tuning was assessed with ILD held constant at the site’s best value and vice versa. By convention, negative ITD and ILD values correspond to left-ear leading and left-ear greater, respectively; positive ITD and ILD values correspond to right-ear leading and right-ear greater, respectively.

ITD tuning curves collected with narrowband stimuli typically had multiple peaks that were separated by integer multiples of the period of the center frequency of the stimulus. For multipeaked tuning curves, further analyses were restricted to the response peak closest to 0 μs unless that peak was less than half the magnitude of another peak. In such cases (6 of the 204 narrowband ITD tuning curves collected), the larger response peak was analyzed.

Optic tectum sampling

Tuning for ITD was also assessed in the optic tecta of the device-reared owls used in this study to verify that adaptive adjustments had occurred in the midbrain pathway. Experience-dependent shifts in ITD tuning were assessed by measuring the relationship between best ITD and VRF azimuth according to a method reported previously (Brainard and Knudsen 1993). VRFs were determined by projecting dark or light bars onto a calibrated translucent hemisphere placed in front of the owl, and the magnitude of shift in ITD tuning at individual sites was determined by comparing the measured best ITD value with the value predicted from the normal relationship between best ITD and VRF azimuth (predicted ITD = VRF azimuth * 2.5 μs/°). Tectal samples were restricted to sites representing frontal space (VRF azimuth within 10° of the midsagittal plane, and VRF elevation between 10° up and 15° down). The shift in ITD tuning for each stimulus (broadband noise and 4, 6, and 8 kHz narrowband noise) was calculated as the shift in best ITD from predicted normal, averaged across all sampled sites.

AAr sampling

In contrast to the topographic representation of ITD and ILD in the midbrain localization pathway (Moiseff and Konishi 1981; Olsen et al. 1989), the representation of ITD and ILD in the AAr has a clustered organization (Cohen and Knudsen 1995). Clusters of neighboring units in the AAr tend to be tuned to similar values of ITD and ILD, but units in different clusters are tuned to dissimilar values. Due to this organization, it is not possible to infer the normal tuning of a unit in the AAr based on its location in the structure. In addition, because units in the AAr do not respond to visual stimuli, the method used in the optic tectum to infer normal binaural tuning from VRF location (see previous section) could not be applied. Therefore to assess the effect of device rearing on the representation of binaural localization cues in the AAr, we compared ITD and ILD tuning across populations of AAr sites from device-reared and normal owls.

The technique used for sampling binaural tuning in the AAr was identical for device-reared and normal owls and was designed to obtain a sample of sites that was representative of the entire population. In each owl, a coarse grid of electrode penetrations was made to determine the extent of the AAr. These grids consisted of series of penetrations separated by 500 μm along the rostrocaudal or mediolateral dimension of the brain. In some cases, additional penetrations were made at locations between the penetrations of the initial grid. All penetrations were separated by at least 250 μm along the rostrocaudal or mediolateral dimension. Within a dorsoventral penetration through the AAr, ITD and ILD tuning was measured at 150- to 250-μm intervals. Sample sizes for an individual AAr ranged from 10 to 34 sites. All measurements reported here were obtained from the AAr on the right side of the brain.

Composite response curves

Composite response curves were constructed as a graphic representation of population ITD or ILD tuning in the AAr. Composite ITD response curves were constructed by calculating the percentage of sampled sites that responded at or above 50% of their maximal response for each of 21 ITD values that spanned the physiological range (~200 to +200 μs) in 20-μs increments. Composite ILD response curves were constructed by calculating the percentage of sampled sites that responded at or above 50% of their maximal response for each of 13 ILD values that spanned the physiological range (30 dB left-ear greater to 30 dB right-ear greater) in 5-dB increments. At some sites, ILD tuning curves were open on one side: these curves contained a single continuous range of ILDs that elicited ≥50% of the maximal response and that extended to either the left-ear greater or right-ear greater limit of the physiological range. In such cases, 30 dB ILD on the open side of the tuning curve was used in place of the 50% cutoff on that side. The weighted average of each composite response curve served as an indicator of population ITD (or ILD) tuning.

RESULTS

Tuning for ITD and ILD was assessed in the right AAr of five normal owls and seven owls raised with the acoustic filtering device in the right ear. Recordings were also made in the right optic tectum of device-reared owls to verify that device rearing had altered binaural tuning in the midbrain localization pathway.

Frequency-specific ITD tuning in the AAr of normal owls

Consistent with previous reports (Cohen and Knudsen 1995), nearly all sites in the AAr of normal owls were tuned for ITD. An example of ITD tuning measured with broadband stimuli is shown in Fig. 2, A and B (top). Sites in the AAr were also tuned for ITD when tested with narrowband stimuli (Fig. 2, A and B, bottom 3 pairs of panels). ITD tuning curves collected with narrowband stimuli typically had multiple peaks that were separated by integer multiples of the period of the center frequency of the stimulus (e.g., 167 μs for 6 kHz and 125 μs for 8 kHz; Fig. 2, A and B, bottom 2 pairs of panels); multiple peaks in broadband tuning curves corresponded to the period of the best frequency for that site. Such multipeaked tuning curves reflect the fact that the auditory system measures ITD from interaural phase differences, which are periodic with respect to time. At this site, ITD tuning was independent of stimulus frequency in that ITD tuning curves collected with 4-, 6-, and 8-kHz narrowband stimuli had a common peak centered at approximately ~35 μs. This peak was similar to the peak of the ITD tuning curve collected with broadband stimuli (~28 μs). The frequency dependence of ITD tuning at this site is summarized in Fig. 2C in which best ITD is plotted for each of the three narrowband stimuli.

Frequency-specific ITD tuning was measured at 48 sites sampled uniformly across the right AAr of five normal owls, as described in METHODS. ITD tuning was largely independent of stimulus frequency at all sites (Fig. 3). Differences among best ITD values measured with 4-, 6-, and 8-kHz narrowband
stimuli at individual sites were small—less than 1 μs, on average—for all stimulus pairs (Fig. 3B).

Most AAr sites were tuned to values of ITD that corresponded with stimuli located in frontal space (Fig. 4). The weighted average of the composite ITD response curve, constructed from broadband ITD tuning curves for all sites (measured on the right side of the brain) was 24 μs left-ear leading. Most sites also responded maximally to small left-ear leading ITD values when tested with narrowband stimuli (Fig. 4, B–D). The weighted averages of the composite ITD response curves based on responses to narrowband stimuli centered on 4, 6, and 8 kHz were −18, −22, and −18 μs, respectively. The con-
stancy of the representation of ITD across frequencies reflects the frequency independence of acoustic ITD produced by sound sources located in frontal space for normal owls (Knudsen et al. 1991).

Frequency-specific ITD tuning in the AAr of device-reared owls

Device rearing altered the frequency dependence of ITD tuning in the AAr. An example of ITD tuning at a site in the AAr of a device-reared owl is shown in Fig. 5. When ITD tuning was assessed at this site using a broadband stimulus, the best ITD value was $-28 \mu s$. In contrast, for a narrowband stimulus centered on 4 kHz, the best ITD value was $-90 \mu s$. For a 6-kHz stimulus, responses could not be evoked at this site even at levels of up to 40 dB above the threshold for 4- and 8-kHz stimuli and regardless of the ILD value used; similarly weak and unreliable responses to 6 kHz stimuli were observed at the majority sites in the AAr of device-reared owls (see following text). For an 8-kHz stimulus, the best ITD value at this site was $-3 \mu s$. Frequency-specific ITD tuning at this site is summarized in Fig. 5C.

ITD tuning was assessed at 58 sites in the right AAr of seven device-reared owls (Fig. 6). The technique for sampling tuning in the AAr was identical to that used in normal owls, as described in METHODS. Like the site in Fig. 5, most sites responded poorly to 6-kHz stimuli even at sound levels well above the threshold for other stimulus frequencies. ITD tuning curves collected with 6-kHz stimuli typically did not contain a distinct response peak regardless of the average binaural level or ILD value used. As a result, ITD tuning for 6-kHz stimuli could be obtained at only 17% (10 of 58) of the sampled sites. Nonetheless, ITD tuning in the AAr of device-reared owls was clearly dependent on stimulus frequency. Best ITDs tended to progress toward right-ear greater values with increasing stimulus frequency (Fig. 6A), and differences among best ITD values measured at individual sites with 4-, 6-, and 8-kHz narrowband stimuli were significantly greater than those observed in normal owls (Fig. 6B).

The range of ITD values represented in the AAr was also altered by device rearing (Fig. 7). ITD tuning for broadband noise was shifted toward more left-ear leading values relative to normal. The weighted average of the composite ITD response curve for broadband stimuli was $-76 \mu s$ compared with $-24 \mu s$ in normal owls. The composite ITD response curves for 4- and 6-kHz narrowband stimuli were also shifted toward left-ear leading relative to normal: the weighted average for 4 kHz was $-63 \mu s$ in device-reared owls compared with $-18 \mu s$ in normal owls, and the weighted average for 6 kHz was $-36 \mu s$ in device-reared owls compared with $-22 \mu s$ in normal owls. ITD tuning for 8-kHz stimuli was shifted in the opposite direction, toward more right-ear leading values in device-reared owls: the weighted average of the composite ITD response curve was $+1 \mu s$ compared with $-18 \mu s$ in normal owls.

The frequency-dependent variation in the representation of ITD across the population of AAr sites in device-reared owls was most apparent when the composite ITD response curves for 4, 6, and 8 kHz were plotted on the same graph (Fig. 8). The shift in the population representation of ITD, as indicated by the difference between the weighted averages of the composite ITD curves from normal and device-reared owls, was $-45 \mu s$ for 4-kHz stimuli, $-14 \mu s$ for 6-kHz stimuli, $+19 \mu s$ for 8-kHz stimuli, and $-52 \mu s$ for broadband stimuli. These shifts were within the range of acoustic shifts caused by the device (Fig. 1A).

The shifts in the composite ITD response curves observed in device-reared owls reflected changes in the distributions of 50% ITD cutoff values (Fig. 9, Table 1). Both flanks of the ITD tuning curves for broadband and 4-kHz narrowband stimuli were shifted significantly toward more left-ear leading ITD values relative to normal. In contrast, the right-ear leading flanks of ITD tuning curves for 8-kHz narrowband stimuli were shifted toward right-ear leading ITD values relative to normal.
Experience-dependent shifts in ITD tuning were assessed in the right optic tecta of the device-reared owls by measuring the relationship between best ITD and VRF azimuth, as described in METHODS. Tectal ITD tuning was shifted by an average of 2.56 ± 1.3 ms (n = 58 sites) for 4-kHz stimuli; 2.35 ± 0.53 ms (n = 9 sites) for 6-kHz stimuli; 1.26 ± 1.1 ms (n = 59 sites) for 8-kHz stimuli, and 2.67 ± 0.44 ms (n = 44 sites) for broadband stimuli. As in the AAr, sites in the tectum responded poorly or not at all to 6-kHz stimuli. As a result, ITD tuning for 6-kHz stimuli could be measured at only 13% (9 of 67) of tectal sites.

Because it was not possible to quantify the magnitude of shifts in ITD tuning at individual sites in the AAr (see AAr sampling), direct comparisons of the relative magnitudes of frequency-specific ITD shifts in the AAr and optic tectum could not be made. However, it was possible to compare directly the frequency dependence of ITD tuning since this measure could be applied in the same manner to both structures (Fig. 10). The mean difference between 4- and 8-kHz best ITD measured at individual sites in the AAr of device-reared owls was 52 ± 23 μs (n = 31 sites) compared with 83 ± 12 μs (n = 51 sites) in the optic tectum. This difference was significant (2-tailed t-test, P < 0.0001), indicating that ITD tuning in the optic tectum exhibited greater frequency dependence than ITD tuning in the AAr of the same owls.

ILD tuning was assessed at 37 sites in normal owls and at 65 sites in device-reared owls. In normal owls, the vast majority of sites in the AAr were tuned to specific values of ILD (Table 2): ILD tuning curves contained a single continuous range of ILDs that elicited more than 50% of the maximal response to a particular narrowband or broadband stimulus, and left and right 50% cutoff values were within the physiological range. Device-reared owls exhibited a greater variety of ILD response functions (Fig. 11, Table 2). Many sites had ILD tuning curves that were open on one side (Fig. 11, B and C): these curves contained a single continuous range of ILDs which elicited more than 50% of the maximal response and extended to either
the left-ear greater or right-ear greater limit of the physiological range (30 dB ILD). In device-reared owls, there were also more sites with ILD tuning curves that did not fit either of these profiles: some sites responded at or above 50% of their maximal response to all ILD values, whereas other sites had more than one range of ILD values that elicited more than 50% of the maximal response. Because of the deterioration of ILD selectivity in the AAr of device-reared owls, it was often not possible to obtain best ILD values for all three narrowband stimuli at individual sites. As a result, it was not possible to quantify the effect of device rearing on the frequency dependence of ILD tuning at individual sites.

Composite ILD response curves were constructed for broadband and narrowband stimuli to provide an indication of the ILD values represented across the population of sampled sites (including sites that were not tuned to a specific value of ILD). In normal owls, most sites in the right AAr were tuned to ILD values near 0 dB, regardless of stimulus frequency (Fig. 12, solid gray curves): the weighted averages of the composite ILD response curves for normal owls for broadband and 4-, 6-, and 8-kHz narrowband stimuli were 2, 1, 0, 2, and 1 dB, respectively.

Device rearing altered the representation of ILD in the AAr. In device-reared owls, composite ILD response curves were shifted toward more left-ear greater values for all four stimuli (Fig. 12, thin black curves): the weighted averages for broadband and 4-, 6-, and 8-kHz narrowband stimuli were −1, 0, −1, and 0 dB, respectively.

Device rearing altered the representation of ILD in the AAr. In device-reared owls, composite ILD response curves were shifted toward more left-ear greater values for all four stimuli (Fig. 12, thin black curves): the weighted averages for broadband and 4-, 6-, and 8-kHz narrowband stimuli were −1, 0, −1, and 0 dB, respectively.
band and 4-, 6-, and 8-kHz narrowband stimuli in device-reared owls were -5, -3, -5, and -6 dB, respectively. Compared to the weighted averages calculated for normal owls, ILD tuning for broadband and 4-, 6-, and 8-kHz narrowband stimuli was shifted by -4, -3, -4, and -5 dB, respectively. These shifts were in the appropriate direction to compensate for the acoustic effects of the device on ILD but were substantially smaller in magnitude than the median acoustic effect of the device (Fig. 1B).

The shifts in the composite ILD response curves observed in device-reared owls reflected changes in the distributions of 50% ILD cutoff values (Table 3; Fig. 13). The mean left and right 50% cutoff values for all four stimuli were nominally shifted toward left-ear greater. However, the distributions of cutoff values were significantly different from normal only for the left-ear greater flanks for broadband and 8-kHz narrowband stimuli. For all stimuli, the mean left 50% cutoff value was farther from the normal mean than was the right 50% cutoff value; this difference was due, in part, to the increase in the number of ILD tuning curves that were open-ended on the left-ear greater side in device-reared owls (Table 2).

**DISCUSSION**

Adaptive adjustment of frequency-specific ITD and ILD tuning in the AAr

These experiments demonstrate that early auditory experience exerts a profound influence on the representation of binaural localization cues in the AAr. Owls raised with the acoustic filtering device exhibited a highly abnormal pattern of frequency-dependent ITD tuning: 4-kHz ITD tuning was shifted toward left-ear leading relative to normal, whereas 8-kHz ITD tuning was shifted in the opposite direction, toward right-ear leading (Figs. 5–9). These changes were adaptive because units became tuned for combinations of frequency-specific ITD and ILD that were appropriate for the acoustic environment in which the owls were raised.

**TABLE 1.** 50% cutoff values for ITD tuning curves in normal and device-reared owls

<table>
<thead>
<tr>
<th>Stimulus Type</th>
<th>n</th>
<th>Left 50% Cutoff Mean, μsec</th>
<th>P†</th>
<th>Right 50% Cutoff Mean, μsec</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>broadband</td>
<td></td>
<td>-45 ± 37</td>
<td></td>
<td>11 ± 33</td>
<td></td>
</tr>
<tr>
<td>Device</td>
<td></td>
<td>-110 ± 56</td>
<td>&lt;0.0001</td>
<td>43 ± 56</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>4 kHz</td>
<td></td>
<td>-47 ± 44</td>
<td>0.0002</td>
<td>10 ± 43</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td></td>
<td>-94 ± 52</td>
<td></td>
<td>-27 ± 44</td>
<td>0.001</td>
</tr>
<tr>
<td>Device</td>
<td></td>
<td>-40 ± 36</td>
<td>0.2204</td>
<td>2 ± 33</td>
<td>0.8367</td>
</tr>
<tr>
<td>6 kHz</td>
<td></td>
<td>-56 ± 36</td>
<td></td>
<td>0 ± 19</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td></td>
<td>-43 ± 32</td>
<td>0.1071</td>
<td>9 ± 30</td>
<td></td>
</tr>
<tr>
<td>Device</td>
<td></td>
<td>-29 ± 45</td>
<td>0.0388</td>
<td>27 ± 43</td>
<td></td>
</tr>
</tbody>
</table>

ITD, interaural time difference; BBN, broadband noise. * Positive values indicate right-ear leading ITDs; negative values indicate left-ear leading ITDs. † Two-tailed t-test.
specific ITD values experienced with the device in place. Device rearing also altered the representation of ILD in the AAr. ILD tuning in device-reared owls was shifted toward left-ear greater values (Figs. 12 and 13). The direction of this shift was appropriate to compensate for the effects of the device on ILD.

Although ITD and ILD tuning shifted in the adaptive direction, the extent to which these shifts were sufficient to compensate fully for the effects of the device is difficult to ascertain. This uncertainty arises in large part because it was not possible to determine the magnitude of tuning shifts at individual sites in the AAr (see AAr sampling). In addition, although the overall pattern of frequency-dependent changes in interaural timing and level imposed by the device is consistent from owl to owl, the magnitude of these changes is not (Gold and Knudsen 1999). Thus although the current results indicate that units in the AAr exhibit adaptive adjustments in frequency-specific binaural tuning, conclusions about the completeness of these adjustments cannot be made with a high level of confidence.

Loss of 6-kHz responses

The loss of responsiveness to 6-kHz stimuli in device-reared owls is remarkable because frequencies near 6 kHz consistently elicit strong responses from units in the AAr of normal owls (Figs. 2–4) (Cohen and Knudsen 1995). A similar decrease in responsiveness to 6-kHz stimuli was also observed in the optic tectum of these owls and has been reported previously (Gold and Knudsen 1999). The authors of the earlier study proposed that this change could have resulted from a long-term deprivation of effective drive from the 6-kHz channel for neurons that are narrowly tuned for ITD and ILD. Because insertion of the device causes large changes in both ITD (median = −29 μs) and ILD (median = −16 dB) for frequencies near 6 kHz, many combinations of ITD and ILD (including combinations of ITD and ILD values near 0, to which most sites in the AAr are normally tuned) cannot be produced from any location in space. As a result, units that are tuned for ITD and ILD, such as those in the AAr and optic tectum, are never driven strongly by frequencies near 6 kHz with the device in place. Long-term deprivation of effective drive from the 6-kHz channel could lead to a loss of responsiveness to 6-kHz stimuli, in a manner analogous to the effects of deprivation of afferent activity on unit responsiveness in primary sensory cortex (visual: Hubel et al. 1977; somatosensory: Kaas et al. 1983; auditory: Robertson and Irvine 1989).

Independent plasticity in the forebrain and midbrain localization pathways

The changes in ITD and ILD tuning observed in the AAr of device-reared owls were similar to those described previously in the optic tectum (Gold and Knudsen 2000a). However, the fundamentally different representations of auditory space in the forebrain and midbrain (clustered vs. mapped) (Cohen and Knudsen 1999) makes it difficult to draw conclusions about the relative magnitudes of adaptive changes in the two pathways. The measure of plasticity that can be compared directly with the greatest confidence is the frequency dependence of ITD tuning, calculated as the average difference between best ITD values measured with 4- and 8-kHz stimuli at individual sites. By this measure, the degree of change in frequency dependence was significantly less in the AAr than in the optic tectum of the same owls (Fig. 10). This difference could be related to differences in the width of ITD tuning in the two structures. ITD tuning widths in the AAr are considerably broader than those in the optic tectum (mean = 68 ± 31 μs in the AAr vs. 46 ± 19 μs in the tectum for 4-kHz ITD tuning; 56 ± 29 μs in the AAr vs. 41 ± 13 μs in the tectum for 8-kHz ITD tuning). Units that are tuned relatively broadly for ITD, such as those in the AAr, would not need to adjust the frequency dependence of their ITD tuning as completely to respond strongly to the abnormal patterns of frequency-specific ITD experienced with the device in place. In contrast, narrowly tuned neurons, like those in the tectum, would have to make relatively larger shifts in their best ITDs to respond strongly to the same abnormal pattern of frequency-specific ITD values.

The difference in the frequency dependence of ITD tuning in the AAr and optic tectum suggests that the changes in binaural tuning observed in the AAr do not result from plasticity in the midbrain localization pathway. This interpretation is supported...
further by the finding that bilateral ablation of the external
nucleus of the inferior colliculus (ICX), the site of plasticity in
the midbrain pathway (Gold and Knudsen 2000b), does not alter
binaural tuning in the AAr (Cohen et al. 1998). The changes in
binaural tuning observed in the AAr of device-reared owls are therefore likely to reflect plasticity within the
forebrain localization pathway.

Comparison of effects of auditory and visual experience

The representation of binaural cues in the AAr is also
influenced by early visual experience (Miller and Knudsen 1999). Raising owls with prismatic spectacles that shift the
visual field in the horizontal plane causes adaptive changes in
broadband ITD tuning in the AAr. Prismatic spectacles and
the acoustic filtering device present different challenges to
the auditory localization pathway, and adaptations to the
two manipulations could involve different mechanisms that
operate at different stages in the forebrain pathway. Prisms
change the correspondence between ITD values and loca-
tions in the visual field without substantially affecting au-
ditory localization cues. The acoustic device, like prisms,
changes the correspondence between cue values and loca-
tions in the visual field. However, in contrast to prisms, the
device also disrupts the representation of auditory space and
alters the range and frequency dependence of binaural cues
(Gold and Knudsen 1999).

For prism-reared owls, the changes in ITD tuning required to
compensate for the optical displacement imposed by the spec-
tacles are essentially the same for all frequencies. Thus adjust-
ments of ITD tuning could occur at a stage in the forebrain
pathway beyond the site at which ITD information is integrated
across frequency channels. In addition, adaptations to the
prisms must involve visually based signals that instruct adjust-
ments of auditory tuning.

For device-reared owls, the required changes in binaural
tuning are frequency specific. Thus plasticity in device-reared
owls must occur at or before the site (or sites) at which ITD and
ILD information is integrated across frequency channels.
Unlike the adaptations to prisms, the adaptations to the acoustic
device do not necessarily require a visual instructive signal.
The modifications of binaural tuning observed in device-reared
owls could be accomplished, for example, by activity-driven
processes that use information contained entirely within the
auditory pathway. Since a sound originating from a particular
location produces a consistent pattern of cues, an appropriate
pattern of frequency-dependent tuning could be acquired by a
Hebbian process that causes units to become tuned to combi-
inations of frequency-specific cue values that occur synchro-
nously.

**TABLE 3. 50% cutoff values for ILD tuning curves in normal and
device-reared owls**

<table>
<thead>
<tr>
<th></th>
<th>Left 50% Cutoff</th>
<th>Right 50% Cutoff</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean,* dB</td>
<td>P†</td>
</tr>
<tr>
<td>BBN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>36</td>
<td>−11 ± 7</td>
</tr>
<tr>
<td>Device</td>
<td>51</td>
<td>−17 ± 10</td>
</tr>
<tr>
<td>4 kHz</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>19</td>
<td>−7 ± 8</td>
</tr>
<tr>
<td>Device</td>
<td>37</td>
<td>−10 ± 13</td>
</tr>
<tr>
<td>6 kHz</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>28</td>
<td>−9 ± 7</td>
</tr>
<tr>
<td>Device</td>
<td>9</td>
<td>−14 ± 9</td>
</tr>
<tr>
<td>8 kHz</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>23</td>
<td>−8 ± 10</td>
</tr>
<tr>
<td>Device</td>
<td>45</td>
<td>−15 ± 12</td>
</tr>
</tbody>
</table>

* Positive values indicate right-ear greater ILDs; negative values indicate
left-ear greater ILDs. † Two-tailed t-test.

**FIG. 12.** Representation of interaural level difference (ILD) in the AAr of normal and device-reared owls. Composite ILD
response curves indicate the percentage of sites that responded at or above 50% of their maximal response for ILDs in the
physiological range. Data from device-reared owls are represented by the solid lines; data from normal owls are represented by the
shaded curves. A: composite ILD response curves for broadband stimuli (normal owls: n = 38 sites; device-reared owls: n = 57
sites). B: composite ILD response curves for 4-kHz stimuli (normal owls: n = 19 sites; device-reared owls: n = 39 sites). C:
composite ILD response curves for 6-kHz stimuli (normal owls: n = 31 sites; device-reared owls: n = 10 sites). D: composite ILD
response curves for 8-kHz stimuli (normal owls: n = 31 sites; device-reared owls: n = 49 sites).

**FIG. 13.** Differences between the mean 50% cutoff values for ILD tuning curves measured in normal and device-reared owls. Bars indicate differences of mean left (□) and right (○) 50% cutoff values between device-reared and
normal owls for 4-, 6-, and 8-kHz and broadband stimuli. Error bars indicate
SE for the distributions from device-reared owls. * conditions for which the distribution in device-reared owls was significantly different from that in
normal owls (2-tailed t-test, P < 0.05, see Table 3).
Comparison to other models of experience-dependent plasticity in the auditory forebrain

Studies of experience-dependent plasticity in the auditory forebrain have focused primarily on changes in frequency tuning or tonotopic organization in the primary auditory cortex (A1) induced by deprivation of afferent input or by behavioral training. For example, physiological recordings in animals trained on tasks that require a behavioral response to tonal stimuli, e.g., frequency discrimination tasks (Edeline and Weinberger 1993; Recanzone et al. 1993) or classical conditioning (Bakin and Weinberger 1999), have revealed increased representations of the behaviorally relevant frequencies in A1 and, in some cases, narrower frequency tuning to those frequencies. Although frequency tuning was not assessed directly in this study, the drastic change in unit responsiveness to 6-kHz stimuli observed in device-reared owls indicates a major reorganization of frequency representation in the AAr.

In addition to this inferred plasticity in frequency representation, device-reared owls exhibited plasticity in the representation of high-order stimulus features, ITD and ILD, which are used to encode the location of auditory stimuli. Another excellent example of experience-dependent plasticity in the representation of high-order stimulus parameters in the auditory forebrain is the emergence of song-selective neurons in the forebrain of songbirds (Douce and Solis 1997; Margoliash 1983; Volman 1993). These studies demonstrate that experience exerts a powerful organizing influence on the representation of high-order stimulus features in the central auditory system.

We are grateful to J. Gold and B. Linkenhoker for comments on an earlier version of this manuscript.

This work was supported by National Research Service Award MH-11238 to G. L. Miller, by National Institute on Deafness and Other Communication Disorders Grant R01 DC-00155-18, and by the March of Dimes Birth Defects Foundation.

REFERENCES


