

Chapter 17

The Auditory Midbrain in Bats and Birds

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1. INTRODUCTION

1.1. EVOLUTION AND PHYLOGENY

Both bats and birds are flying vertebrates that diverged early in evolution. Their flight mechanisms are different, and so are their auditory systems. They share a common ancestor in the Carboniferous era, but their auditory systems evolved in parallel and are not homologous (Clack 1997). However, other ancestral mammalian traits, such as moveable ears, multiple ossicles, and echolocation have modified the ear and the auditory system of bats. We discuss both species because they reveal neuroethological principles that relate neural activity to behavior.

1.2. BEHAVIORAL CONTEXT

Bats and birds use hearing to localize and analyze sound sources passively, and to communicate with conspecifics (Kanwal et al. 1993; Konishi 2000). Some birds learn song and have forebrain areas to control vocal pathways. Others, like the barn owl, are nocturnal predators with superb sound localization skills. Bats use their extraordinary hearing in concert with stereotyped vocalizations and listen to the echoes from objects. By analyzing how echoes have been modified from the original sound by reflective objects, bats perceive obstacles and capture flying insects in darkness.

1.2.1. Bat Hearing and Echolocation

Bats are Chiroptera, an order closely related to insectivores. Because bats use their sense of hearing to perform tasks that in other mammals are guided by vision, their auditory system has undergone a corresponding species-specific hypertrophy and specialization (Neuweiler 1990). The inferior colliculus (IC) is a structure critical for hearing that has evolved to fulfill unique functional needs for different species of bats.

There are approximately 1000 bat species and each uses a different pattern of vocalization for echolocation (Neuweiler 2000). Bats that hunt for insects in open spaces (e.g., the Mexican free-tailed bat, *Tadarida brasiliensis*) use short-duration frequency-modulated (FM) calls. Bats that hunt in foliage use calls with a long constant-frequency (CF) component and a short FM component (CF-FM calls). The best studied CF-FM species are the mustached bat, *Pteronotus parnellii*, and the horseshoe bats, *Rhinolophus rouxi* and *R. ferrumequinum*. Other species, like the big brown bat, *Eptesicus fuscus*, use either CF- or FM-type calls (Fig. 17.1) depending on circumstances (Simmons 1989; Grinnell 1995).

Bat echolocation calls are modified in predictable ways by objects. The interval between call and echo is proportional to the distance of the reflective object. The attenuation of the echo depends on the object's size and distance. Three-dimensional structures create characteristic interference patterns in the echoes (Simmons 1989). The IC contains neurons sensitive to all these features of echolocation signals.

All bat species listen to sounds passively and most echolocate. Species that glean from surfaces such as the pallid bat, *Antrozous pallidus*, listen to sounds made by prey (Fuzessery et al. 1993). Many bat species have a rich repertoire of communication sounds that differ from echolocation calls in temporal structure (Kanwal et al. 1993).

Because there is so much information on the patterns of sound that are behaviorally relevant, bats have become an important model system in which to study temporal aspects of sound processing. Although bats are specialized mammals, much of what has been learned about their auditory systems can be generalized to other mammals (Covey 2003).

1.2.2. Avian Hearing

Psychophysical tests have measured auditory sensitivity, loudness, and temporal resolving power in several species of birds. These data resemble those for other vertebrates, including humans (Dooling et al. 2000). Birdsong has become a model for complex sound processing, especially in the auditory midbrain (Theunissen et al. 2000). Studies of the owl, a sound-localization specialist, have implications for spatial hearing, while the development of the map of auditory space has become a paradigm for studies of experience-dependent plasticity (Knudsen 2002).

1.2.3. The Auditory Midbrain: A Hub of the Central Auditory System

In birds and mammals, the midbrain occupies a central position in the auditory system, receiving input from many ascending and descending sensory pathways as well as motor and modulatory projections. The IC projects to the thalamus and has abundant motor and premotor targets (Covey and Casseday 1995; Carr and Code 2000). Besides developing selectivity for biologically relevant sounds, the IC likely transforms the high rate of auditory input into a slower rate of

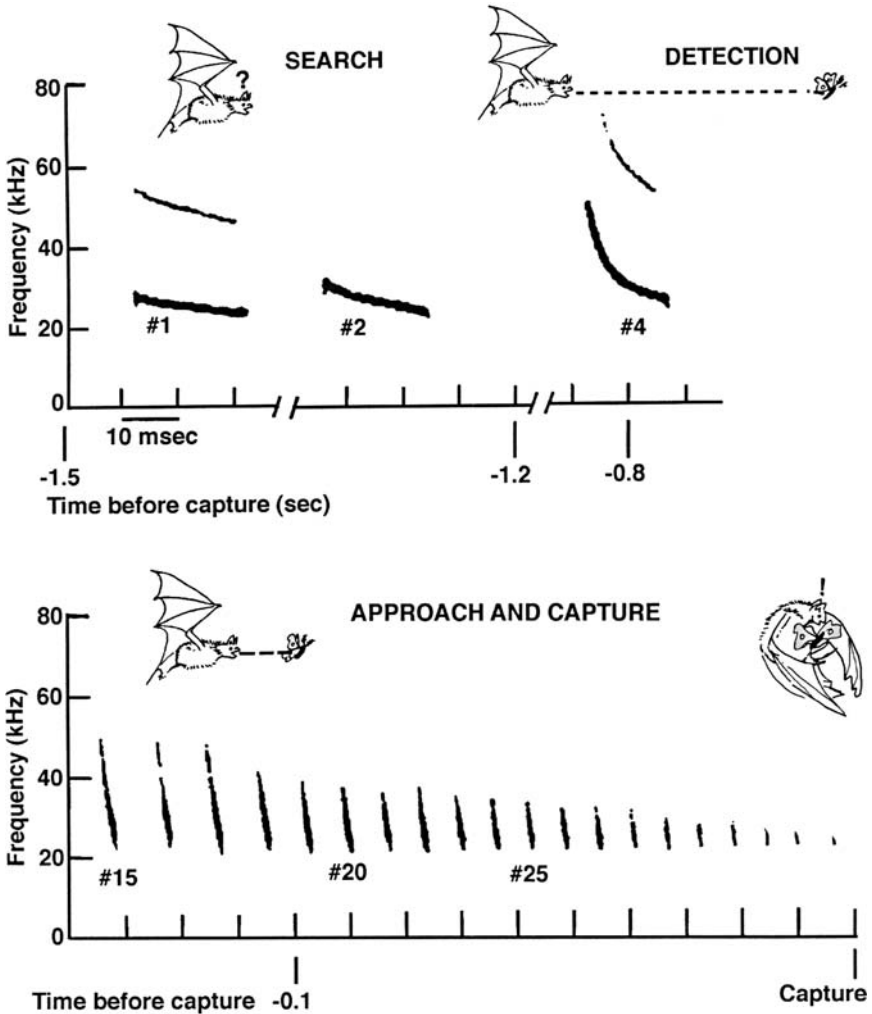


Figure 17.1. Echolocation calls of *Eptesicus* during foraging, pursuit, and insect capture. Calls are 100 dB SPL or more. While hunting the bat emits narrowband quasi-constant frequency calls (#1, #2) between 23 and 29 kHz and up to 20 ms or longer. After finding an insect, it emits broadband FM calls (#4 to #25) that decrease in duration and increase in rate until the terminal buzz (#25 to end) when durations are <1 ms and the repetition rate is up to 150/s. (From Simmons 1989; redrawn from Casseday and Covey 1995.)

output that matches the speed of motor performance (Casseday and Covey 1996).

2. INFERIOR COLLICULUS STRUCTURE

2.1. STRUCTURE AND CHEMOARCHITECTURE OF THE BAT INFERIOR COLLICULUS

The bat IC is enormous and protrudes between the cerebellum and the cortex. In Nissl-stained material it does not have obvious subdivisions (Fig. 17.2), although most species have a “pericentral” area that contains large neurons and

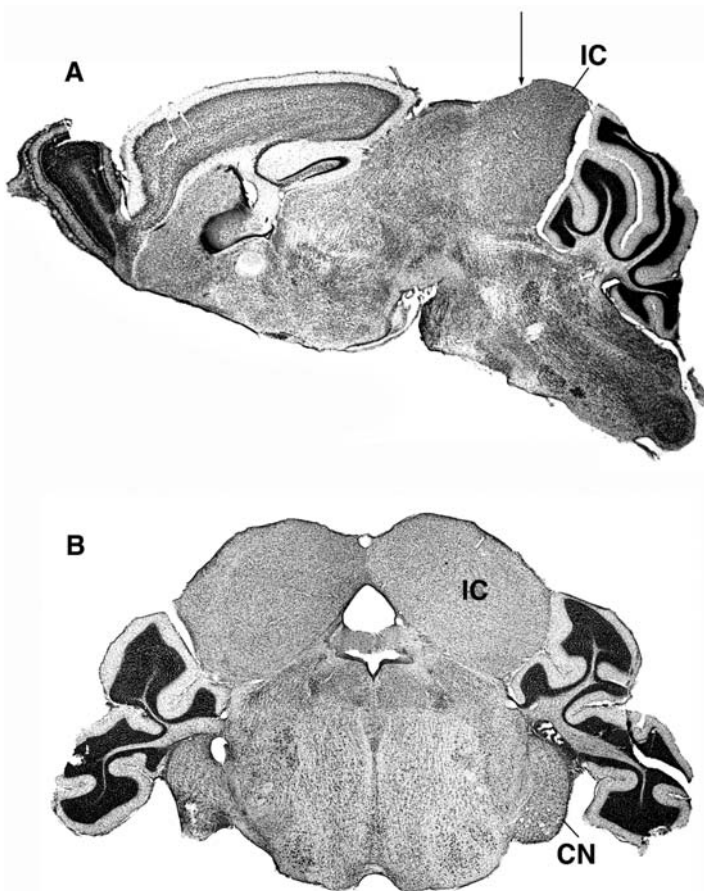


Figure 17.2. Nissl preparations showing the relative size and location of the IC in an echolocating bat, *Eptesicus fuscus*. (A) Parasagittal section. (B) Frontal section through the caudal one-third of the IC; the caudorostral level is indicated by the arrow (A).

probably corresponds to the external nucleus in other mammals (see Chapter 22).

2.1.1. Organization of the Bat Inferior Colliculus

Like that of other mammals, the bat IC contains various cell types, including small disc-shaped cells and large multipolar neurons (Zook et al. 1985; see Chapter 22). *Eptesicus* and other bats with a flexible repertoire of echolocation calls and behavior have a homogeneous IC. *Pteronotus*, a CF-FM bat, has an expanded region of the basilar membrane, the “auditory fovea” (Pollak et al. 1972; Bruns and Schmieszek 1980). There is a corresponding IC “foveal” frequency presentation that is distinguished cytoarchitecturally, the dorsomedial (or dorsoposterior) division (Zook and Casseday 1982; Zook et al. 1985).

2.1.2. Biochemical Gradients in the Bat Midbrain

Chemoarchitectural markers reveal regional differences or gradients within the IC. Immunoreactive synaptic endings (puncta) stained for the inhibitory neurotransmitter γ -aminobutyric acid (GABA) are virtually absent in a crescent-shaped area in the ventrolateral IC, but this same area is immunostained for glycine (Vater et al. 1992b; Winer et al. 1995). Local gradients in GABA and glycine immunoreactivity are organized so that each area is devoted to a single frequency range. This specific isofrequency lamina contains subregions in which neuroactive compounds are abundant or sparse. The distribution of GABA_A and glycine receptors follows the distribution of GABA and glycine puncta; however, GABA_B receptors are concentrated in the dorsomedial IC (Fubara et al. 1996). Because GABA_A receptors provide rapid inhibition and GABA_B receptors subserve longer inhibition, the same neurotransmitter could have different effects in different IC subregions.

The IC receives glutamatergic excitatory input from many sources in the cochlear nucleus (CN) and superior olivary complex (SOC) and modulatory input from neurons containing acetylcholine (Habbicht and Vater 1996) or serotonin (Kaiser and Covey 1997; Hurley and Thompson 2001). Serotonin concentrates in the dorsomedial half of the IC and at the lateral edge.

Other biochemical markers include the Ca²⁺ binding proteins, parvalbumin, calbindin-D28 and calretinin (Zettel et al. 1991; Vater and Braun 1994), and the voltage-gated potassium channel subunit, *Kv1.1* (Rosenberger et al. 2003). Parvalbumin is present in many neurons of all types throughout the IC. Calbindin- and calretinin-positive neurons are concentrated in the dorsomedial IC and external nucleus. Calretinin-positive fibers are densest in an arc above the glycine-rich area, probably from heavy input from calretinin-positive cells in the ventral nucleus of the lateral lemniscus (VLL), which are also glycinergic (Vater et al. 1997).

The *Kv1.1* potassium channel subunit is related to ion channel kinetics implicated in precise temporal processing (Brew and Forsythe 1995). Neurons immunoreactive for *Kv1.1* in *Eptesicus* are mostly in the ventral two thirds of the

IC, decreasing from ventrolateral to dorsomedial (Rosenberger et al. 2003). Many immunolabeled cells are multipolar, indicating that disc-shaped cells have few or no *Kv1.1* ion channels. This regional concentration suggests that multipolar neurons in the ventrolateral IC are distinct and concerned with preserving precise timing.

2.2. STRUCTURE OF THE AUDITORY MIDBRAIN IN BIRDS

The avian auditory midbrain forms when a caudodorsal portion of the mesencephalic vesicle buckles and thickens to encroach upon the tectal ventricle (Puelles et al. 1994). This massive invagination protrudes beneath the tectal ventricle as the torus semicircularis in nonmammalian species. The torus contains three main parts: the intercollicular area, the toral nucleus, and the preisthmic superficial area (Puelles et al. 1994; Fig. 17.3). The toral nucleus includes the auditory region. It is surrounded rostrally and laterally by the intercollicular area (Wild et al. 1993) and caudally by the caudal preisthmic superficial area (Puelles et al. 1994).

Auditory midbrain nomenclature varies by author and custom. The main recipient of ascending auditory information, Puelles' toral nucleus, has been referred to as the mesencephalic lateral nucleus, pars dorsalis (MLd) (Karten 1967) and as the inferior colliculus (Knudsen 1983). We use the term inferior colliculus, as a major premise of this account is that the functional organization of the avian auditory midbrain parallels that of the mammalian IC.

IC borders and connections have been reevaluated and an intercollicular area between the IC and the tectum identified (Puelles et al. 1994; Fig. 17.3). The intercollicular core, also called DM in songbirds, mediates avian call production and has robust cholinergic immunoreactivity and steroid binding sites (Balthazart 1992; Gahr et al. 1993). Consistent with its function in call production, the intercollicular core receives descending input from the lateral hypothalamus and forebrain archistriatum, specifically the robust archistriatal nucleus, which provides descending motor control of the songbird vocal organ (Wild et al. 1993).

2.2.1. Organization of the Avian Inferior Colliculus

The avian IC contains a large tonotopically organized central nucleus (ICC) and two surrounding nuclei. The central nucleus contains a central core (ICCc) surrounded by lateral (ICCLs) and medial (ICCMs) shells. Lateral to the central nucleus is the external nucleus (ICX). Surrounding ICC and ICX dorsally is a periventricular lamina, the superficial nucleus (ICS; Wagner et al. 2003). Medial to the ICC is the caudomedial shell and paracentral nucleus, both intercollicular structures (Fig. 17.3B; Puelles et al. 1994).

2.2.2. Neurons and Internal Organization

The bird IC, like that of the bat, contains many large, loosely packed cells with fusiform, stellate, or round somata (Knudsen 1983). In Golgi preparations many

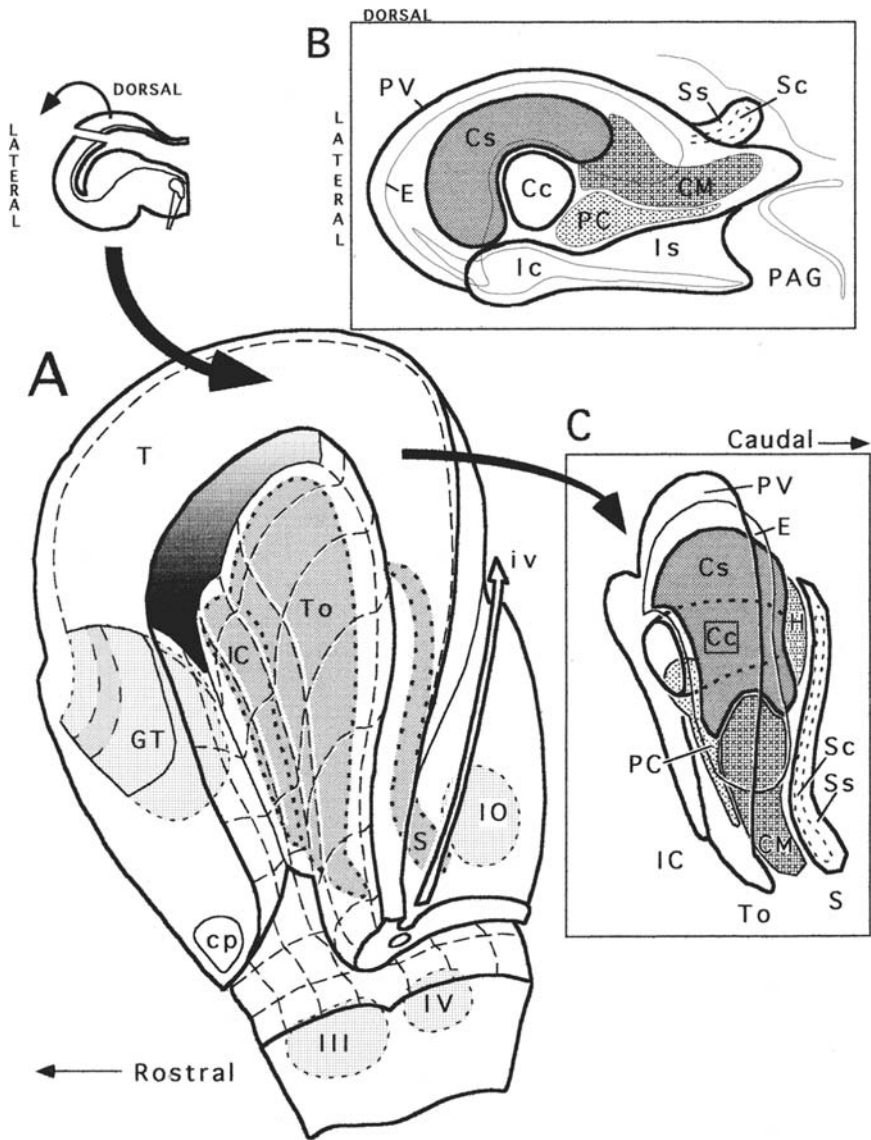


Figure 17.3. Avian auditory midbrain organization. The inset (upper left) partially removes the mesencephalic roof. (A) Schema of the right torus protruding into the optic lobe ventricle, showing its topographic relationships with tectum (*T*), tectal gray (*GT*), and isthmic structures: isthmo-optic nucleus (*IO*) and trochlear nerve (*iv*). The three toral subdivisions (*IC*, *To*, *S*) are shaded dotted contours; black arrow denotes subdivisions (cf. C). (B) Subdivisions of the right torus from a rostral perspective as projected in a transverse plane (directional arrows: dorsal and medial) and related to the paracentral toral nucleus (*PC*), external toral nucleus (*E*), toral periventricular lamina (*PV*), intercollicular area core (*Ic*) and shell (*Is*), periaqueductal gray (*PAG*), preisthmic superficial area shell and core (*Ss*, *Sc*), and preisthmic dorsal brain surface (right). (C) Toral nucleus subdivisions (as in A) showing the posterior location of the hilar nucleus (*H*) and the orientation of the central core (*Cc*). (Modified from Puelles et al. 1994.)

cells are multipolar with stellate or elongate somata (Fig. 17.4). Bipolar and unipolar cells are rare and lie near the margins of the nucleus. Unlike most mammals (see Chapter 2), there is neither fibrodendritic alignment nor preferred orientation. Dendritic fields may be polarized in any dimension and the lemniscal input does not enter or ramify in a laminar fashion (Knudsen 1983). External nucleus cells are smaller than those in the central nucleus, but the same cell types occur.

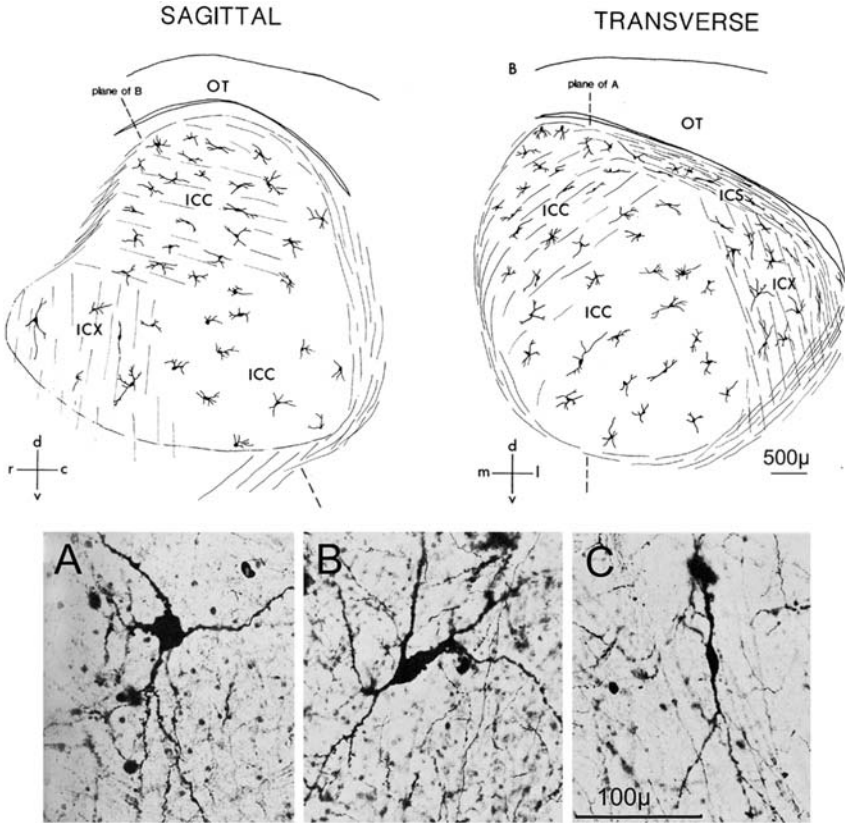


Figure 17.4. IC cell types and subdivisions in Golgi preparations. *Fine lines*, fibers; *ICC*, IC central core, dorsal and ventral; *ICS*, IC superficial nucleus; *ICX*, IC external nucleus; *OT*, optic tectum. (A) ICX stellate cell. (B) ICX elongate cell. (C) ICS bipolar cell. (Modified from Knudsen 1983.)

2.2.3. Biochemical Gradients in the Bird Inferior Colliculus

Biochemical features delineate and support the scheme of architectonic divisions (Fig. 17.5). The differential distributions of these markers identify nuclear subdivisions, which are more apparent than in bats.

In the barn owl and chicken, calretinin immunoreactive fibers from the nucleus laminaris demarcate the laminaris terminal field in the ICCc and thus the pathway used for interaural time difference (ITD) computations (Puelles et al. 1994; Takahashi et al. 1987; Kubke et al. 1999). Acetylcholinesterase defines the medial and lateral shell, and the interaural level difference (ILD) pathway (Adolphs 1993; Puelles et al. 1994). Other markers label other IC subdivisions, including the ICX and ICS (Puelles et al. 1994; Wagner et al. 2003).

GABAergic inhibition is a hallmark of the IC in all vertebrates, including birds (Carr et al. 1989; Fujita and Konishi 1991; Müller 1988; Zheng and Knudsen 1999). ICC contains both the largest number and the largest GABAergic neurons. Cytochrome oxidase distinguishes chicken ICCc from a moderately active ICX (Dezso et al. 1993) and the lateral shell had stronger neuropil reactivity than the central core.

3. CONNECTIONS OF THE INFERIOR COLLICULUS

3.1. CONNECTIONS OF THE INFERIOR COLLICULUS IN BATS

3.1.1. Afferent Inputs

An enormous variety of projections converge in the IC (Fig. 17.6) (Covey and Casseday 1995; Casseday et al. 2002) and brain stem input extends nearly to the IC surface laterally and dorsally. This section focuses on characteristic features in the context of the physiology of the inputs (see Chapters 2 to 5).

Monaural projections (Fig. 17.6A) arise in the contralateral cochlear nucleus (CN), and indirectly from the ventral (VLL) and intermediate (ILL) nuclei of the lateral lemniscus. Binaural projections come from the medial superior olive (MSO), lateral superior olive (LSO), and dorsal nucleus of the lateral lemniscus (DLL). These projections converge throughout the IC with varying degrees of overlap. Dorsal cochlear nucleus (DCN) input extends through almost all of the IC, and is densest in the dorsomedial one third. Posteroventral cochlear nucleus (PVCN) projections are more prominent than in other mammals, and are uniformly distributed. Input from the anteroventral cochlear nucleus (AVCN) is dense ventrolaterally, declining dorsomedially (Zook and Casseday 1985, 1987).

ILL and VLL are hypertrophied and highly specialized in all species of bats (Covey 1993). The VLL of echolocating bats contains a segregated, functionally specialized population of small neurons, the columnar nucleus (VLLc) (Covey and Casseday 1986, 1991), whose neurons are segregated, permitting their inputs to be readily examined. Each sheet receives convergent input from many CN

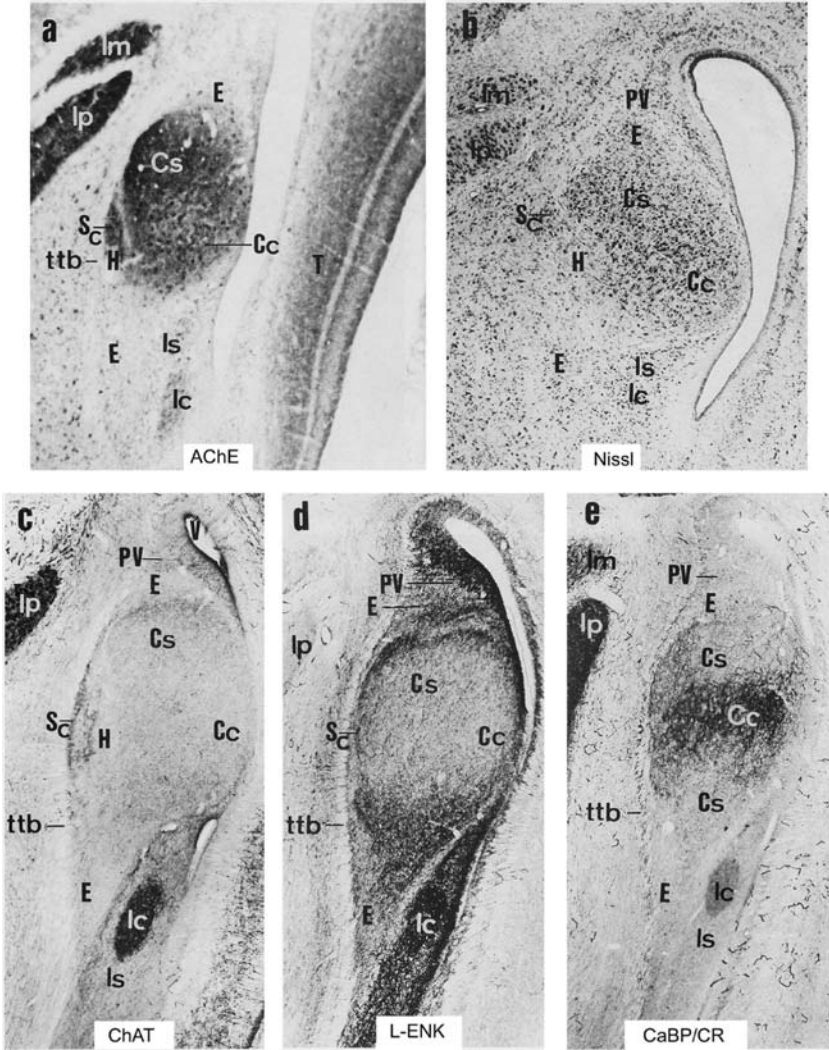


Figure 17.5. Chick IC chemoarchitecture in sagittal sections through the central nucleus core (*Cc*). Dorsal is up, rostral to the right. (A) Acetylcholinesterase (*AchE*). (B) Nissl stained section. (C) Choline acetyltransferase (*ChAT*). (D) L-Enkephalin (*L-Enk*). (E) Calcium binding protein and/or calretinin. *Cc*, IC central core; *Cs*, IC shell; *E*, external nucleus; *H*, hilar toral nucleus; *Ic*, intercollicular area core; *Im*, nucleus isthmi, pars magnocellularis; *lp*, nucleus isthmi, pars parvicellularis; *Is*, intercollicular area shell; *PV*, toral periventricular lamina; *Sc*, preisthmus superficial area core; *T*, optic tectum; *ttb*, tectobulbar tract. (Modified from Puelles et al. 1994.)

cells, which represent a broad range of frequencies and project to an equally broad IC territory (Covey and Casseday 1986). The VLLc projection is the most dense and widespread of IC inputs. VLLc neurons are glycinergic, so presumably provide widespread inhibition (Vater et al. 1997). The projections of ILL and the remainder of VLL extend throughout the IC and overlap those of VLLc (Covey and Casseday 1986).

Binaural projections originate from LSO and DLL bilaterally, and MSO ipsilaterally (Fig. 17.6B) (Casseday et al. 1988; Vater et al. 1995) except in *Tadarida*, whose MSO input is bilateral (Grothe et al. 1994). The MSO in most bats probably serves a different function than MSO in species with prominent low frequency hearing (Casseday et al. 1988; Covey et al. 1991; Grothe et al. 1992). Instead of processing interaural time differences, which in bats are probably too small to be a useful cue for sound location, the MSO may represent the amplitude envelope of a high frequency carrier (Grothe et al. 1992). The MSO, LSO, and DLL projections extend throughout IC and overlap with each other and with monaural input (Zook and Casseday 1987; Covey et al. 1991; Vater et al. 1995). Although inputs converge, those from each source form gradients: DCN predominates in the dorsomedial part of each isofrequency lamina, while AVCN, LSO, and NLL predominate ventrolaterally.

3.1.2. Other Afferents

Mammalian IC receives projections arising from auditory cortex (Herbert et al. 1991; Winer et al. 1998), parts of the medial geniculate body (MGB) and posterior thalamus (Senatorov and Hu 2002), and the substantia nigra pars reticulata, globus pallidus, and central gray (Winer et al. 2002). Most of these pathways have not been studied in bats. In *Pteronotus*, layer V cells in auditory cortex project to the dorsomedial IC but not to the ventrolateral part. Input from the basal amygdaloid nucleus in *Pteronotus* and *Antrozous* (Marsh et al. 2002) is distributed throughout most of the IC.

3.1.3. Projections of the Inferior Colliculus

The IC projects to the MGB (Wenstrup et al. 1994; see Chapter 7) and to the superior colliculus (Covey et al. 1987) and pontine gray (Frisina et al. 1989; Schuller et al. 1991; Wenstrup et al. 1994). Input to the pontine gray is comparable in size to the tectothalamic path, suggesting that auditory input to the cerebellum is crucial for aerial species that echolocate.

3.2. CONNECTIONS OF THE AVIAN INFERIOR COLLICULUS

Avian IC projections follow the same pattern as other vertebrates, with brain stem input terminating topographically in the contralateral IC (Fig. 17.7; Carr and Code 2000). The surrounding intercollicular area receives descending input from the forebrain archistriatum (Puelles et al. 1994; Wild 1995).

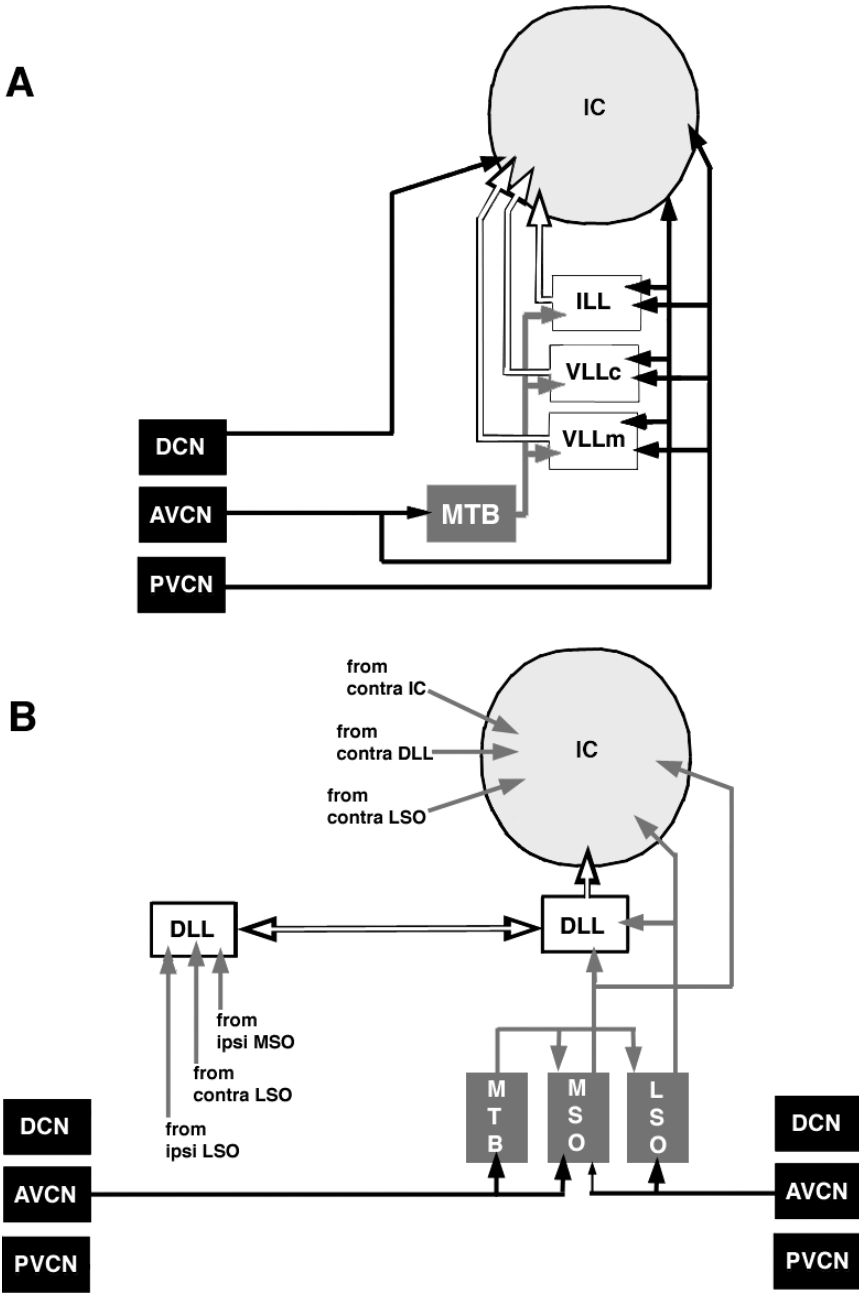


Figure 17.6. Ascending projections to the bat IC. **(A)** Monaural direct and indirect CN pathways to contralateral IC. **(B)** Binaural input from both CN via the superior olivary complex and DLL. *AVCN*, Anteroventral cochlear nucleus; *DCN*, dorsal cochlear nucleus; *DLL*, dorsal nucleus of the lateral lemniscus; *IC*, inferior colliculus; *ILL*, intermediate nucleus of the lateral lemniscus; *LSO*, lateral superior olive; *MSO*, medial superior olive; *MTB*, medial nucleus of the trapezoid body; *PVCN*, posteroventral cochlear nucleus; *VLLc*, ventral nucleus of the lateral lemniscus, columnar division; *VLLm*, ventral nucleus of the lateral lemniscus, multipolar cell division (modified from Woolley and Casseday 2004; see also Karten 1968; Schwartz et al. 1995).

3.2.1. Afferent Inputs

There are two lemniscal projections to the ICC, one from the cochlear nucleus angularis (NA) and another from the cochlear nucleus magnocellularis (NM). The NA projection is direct. The NM projects solely and bilaterally to the brain stem nucleus laminaris (NL) where ITD sensitivity first arises, and the NL projects to the IC. Thus, the NL input is analogous to the mammalian MSO projection. Selective, reversible ablation of each cochlear nucleus shows that the two ascending streams form separate neural channels to encode time and intensity cues for sound localization. Injection of local anesthetic in NM alters the space-specific cells' selectivity for ITD, leaving their ILD selectivity intact. Anesthetizing NA has the opposite effect (Takahashi et al. 1984).

Indirect pathways from the avian SO and lateral lemniscal (LL) nuclei also project to the ICC (Fig. 17.7; Leibler 1975; Conlee and Parks 1986; Takahashi and Konishi 1988a,b; Takahashi et al. 1989; Adolphs 1993). The NL and NA projections are segregated within the ICC, perhaps more so in the barn owl than in the chicken or pigeon (Conlee and Parks 1986; Wild 1995). In the barn owl, the ICC core receives ITD input from the contralateral NL and anterior DLL (Takahashi et al. 1987; Takahashi and Konishi 1988a; Adolphs 1993; Carr and Code 2000). Contralateral NA projects to the lateral and medial shell, conveying both ILD and other information. The lateral shell also receives ITD input from the contralateral core (Takahashi et al. 1989). These ITD and ILD signals converge in the lateral shell, which in turn projects to the ICX (see Section 5). Most of the avian auditory system to the level of the midbrain is binaural and without the specialized monaural pathways found in mammals.

3.2.2. Projections of the Avian Inferior Colliculus

The ICC projects to both the ICX and the thalamic nucleus ovoidalis (Fig. 17.7; Proctor and Konishi 1997; Carr and Code 2000). The ICX projects to the optic tectum where the auditory and visual maps are in register (Knudsen 1983). In the barn owl, the ICX also receives a topographic, visually based instructive signal from the tectum which calibrates the auditory space map (Luksch et al. 2000; Hyde and Knudsen 2002; see Section 6).

Auditory–motor connections are essential for bird vocalizations. The intercollicular area receives auditory input from the IC in the dove (Akesson et al. 1987) and is part of the descending telencephalic archistriatal pathway for vocal control (Wild 1993; see also Jarvis et al. 2000). The ICX projects to the deep layers of the tectum, which projects to the pontine tegmentum, enabling orientation to sound in space (Knudsen and Knudsen 1983; Knudsen et al. 1993). In birds, the connections of the IC to the tectum are probably concerned with sound localization, and in generating the nontotopic space map in the ICX. The tonotopically organized representation that is transferred to the thalamic pathway in both birds and bats may be concerned with other aspects of sound processing (Bonke et al. 1979; Durand et al. 1992).

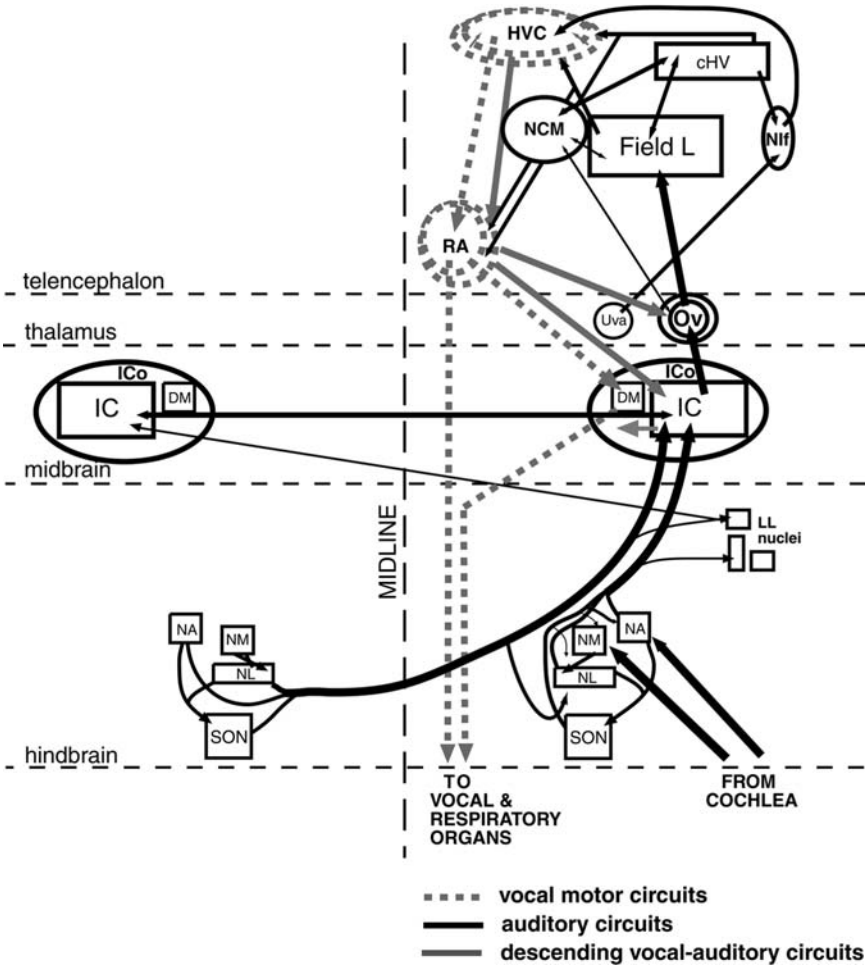


Figure 17.7. Connections of the avian IC. Typical avian auditory system and the passerine song control nuclei. Ascending auditory circuits, *black*; *dashed gray lines*, main descending song control circuit; *solid gray lines*, descending input from the song nuclei (HVC shelf and RA cup) to MLd and Ov. *cHV*, Caudal hyperstriatum ventrale; *DM*, dorsal mesencephalic nucleus and part of ICo; *HVC*, hyperstriatum ventrocaudal (used as a proper name); *IC*, inferior colliculus; *ICo*, nucleus intercollicularis; field L, forebrain auditory area; *LL nuclei*, lateral lemniscal nuclei; *NA*, nucleus angularis; *NCM*, caudo-medial neostriatum; *Nif*, nucleus interfacialis; *NL*, nucleus laminaris; *NM*, nucleus magnocellularis; *Ov*, nucleus ovoidalis; *RA*, robust nucleus of the archistriatum; *SON*, superior olivary nucleus; *Uva*, nucleus uvaeformis of the thalamus. IC receives parallel inputs from lower brain stem and projects to the auditory thalamus (*Ov*), as does the ventral nucleus of the lateral lemniscus. (Modified from Woolley and Casseday 2004; see also Karten 1968; Wild 1987; Schwarz et al. 1995; Wild et al. 1997, 2001.)

4. TONOTOPIC ORGANIZATION OF THE INFERIOR COLLICULUS

4.1. TONOTOPIC ORGANIZATION IN BATS

The bat IC, like that of other mammals, is tonotopically organized with low-frequency afferents terminating dorsolaterally and high-frequency input ventromedially. Many bat species have expanded representations of specific frequency ranges that are critical in echolocation (Fig. 17.8).

4.1.1. Tonotopy in Frequency Modulating Bats

Eptesicus is a species without cochlear specializations. The largest area in the ICC is the 20- to 40-kHz representation, with a continuous low-to-high sequence from dorsolateral to ventromedial (Casseday and Covey 1992). *Antrozous* uses echolocation and passive listening to detect and locate prey. IC tonotopy resembles that in *Eptesicus* except that there is a larger representation below 20 kHz and no expanded isofrequency contour. IC regions devoted to echolocation (30 to 60 kHz) and passive listening (<30 kHz) are segregated, with the dorsal and lateral regions serving passive listening and the ventral region serving echolocation (Fuzessery and Hall 1999).

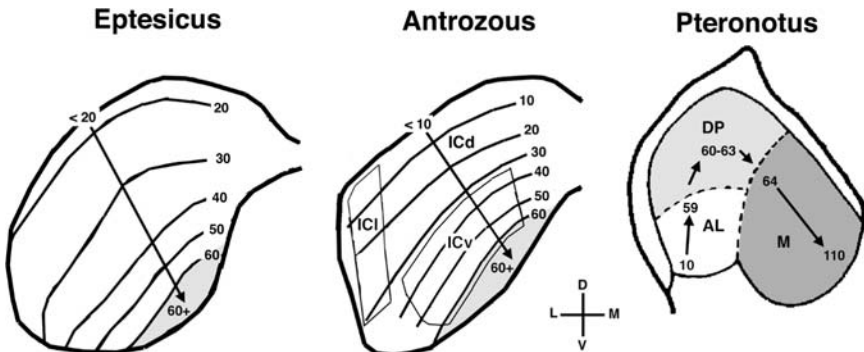


Figure 17.8. Tonotopic organization in the left IC of three species of bats. *White areas*, frequencies <60 kHz; *gray areas*, >60 kHz. In *Pteronotus*, the light gray area is the expanded 60-63 kHz region and the dark gray area is 64 kHz and higher. *Arrows*, tonotopic axis from low-to-high frequency. In *Antrozous*: *ICd*, dorsal IC region; *ICl*, lateral IC region; *ICv*, ventral IC region. In *Pteronotus*: *AL*, Anterolateral region IC; *DP*, dorsal posterior IC region; *M*, medial IC region. Orientation: *d*, dorsal; *l*, lateral; *m*, medial; *v*, ventral.

4.1.2. Specialized Tonotopy

The cochlear specializations in *Pteronotus* bias the auditory system at every level toward the second harmonic of the CF echolocation signal, at about 61 kHz (Kössl and Vater 1985; Henson and Henson 1991; Kössl et al. 1999). Thus, 61 kHz occupies its expected place in subcollicular tonotopic sites (Vater et al. 1985; Zook and Leake 1989). However, in the IC, this region is displaced to form the dorsoposterior region (DP), and frequencies >63 kHz are expanded concomitantly, forming a large medial division (M) while those <60 kHz are greatly reduced (Pollak and Casseday 1989). To accommodate this expansion, the sequence is convoluted and semicircular. However, in *Rhinolophus*, another CF-FM bat with an “acoustic fovea” created by cochlear specializations, ICC frequency organization resembles that in FM bats and other mammals (Rübsamen and Schäfer 1990).

4.2. TONOTOPY IN THE AVIAN INFERIOR COLLICULUS

Birds have an IC tonotopic orientation like that in mammals (Carr and Code 2000) with low best frequencies dorsally and higher frequencies ventrally (chicken: Coles and Aitkin 1979; guinea fowl: Heil and Scheich 1986; owl: Wagner et al. 1987, 2002; zebra finch: Woolley and Casseday 2004). There is a monotonic relationship between best frequency and recording depth, although best frequency changes more slowly in the low-frequency region (Wagner et al. 2002).

Owl ICCc frequency tuning curves are typically single peaked and symmetrical, with steep slopes on both flanks (Fig. 17.9A–C). Tuning curve widths are related to best frequency (BF), such that the ratio of tuning width to BF decreases as BF increases (Wagner et al. 2002). They are also related to IC subdivisions: lateral shell neurons have broader tuning curves and ICX cells prefer noise (Knudsen and Konishi 1978; Wagner et al. 1987; Mazer 1997). In the chicken and zebra finch, BFs range from 1 to 6 kHz and tuning curve widths are variable (Coles and Aitkin 1979; Woolley and Casseday 2004; Fig 17.9D–F). Most zebra finch IC neurons have V-shaped tuning curves, with a quarter having multiple peaks, noncontiguous excitatory regions, or narrow tilted or columnar shapes. Double peaked tuning curves occur in about 12% of chicken neurons (Coles and Aitkin 1979), and single- and multi-peaked tuning curves are found in awake guinea fowl (Scheich et al. 1977). Temporal response patterns in the chicken and zebra finch revealed several categories (Coles and Aitkin 1979; Woolley and Casseday 2004). In anesthetized finches, 49% of IC neurons had onset responses, 20% primary-like, 19% sustained, and 12% primary-like with notch (Woolley and Casseday 2004).

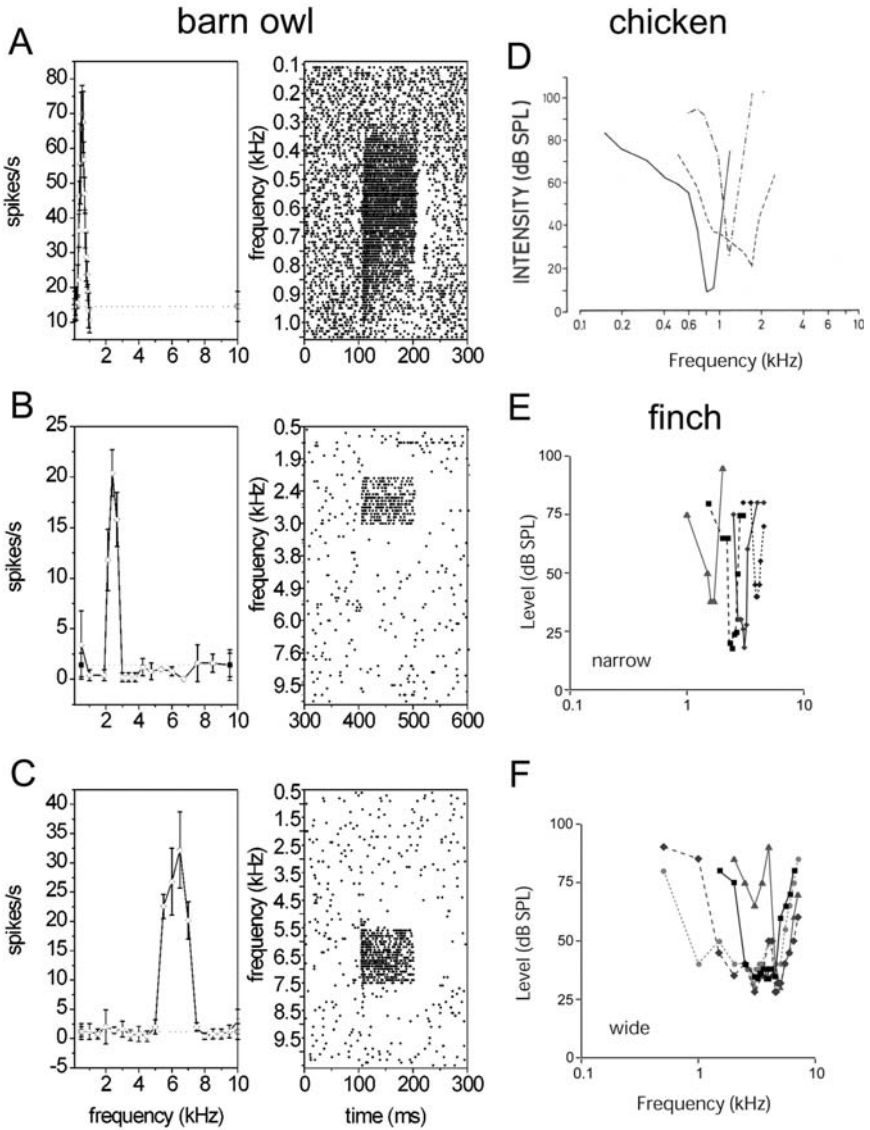


Figure 17.9. Avian IC tuning curves. (A–C) The barn owl ICC is tonotopic with best frequency increasing from dorsal (A) to ventral (C). *Left column*, isointensity frequency response functions with pure tone stimuli. *Right column*, dot raster plots for the same response functions. (D–F) Excitatory tuning curves for chicken and zebra finch. (D) Mid-frequency tuning curves in chicken. Narrow (E) and broad (F) tuning curves in zebra finch. (From Coles and Aiken 1979; Wagner et al. 2002; and Woolley and Casseday 2004.)

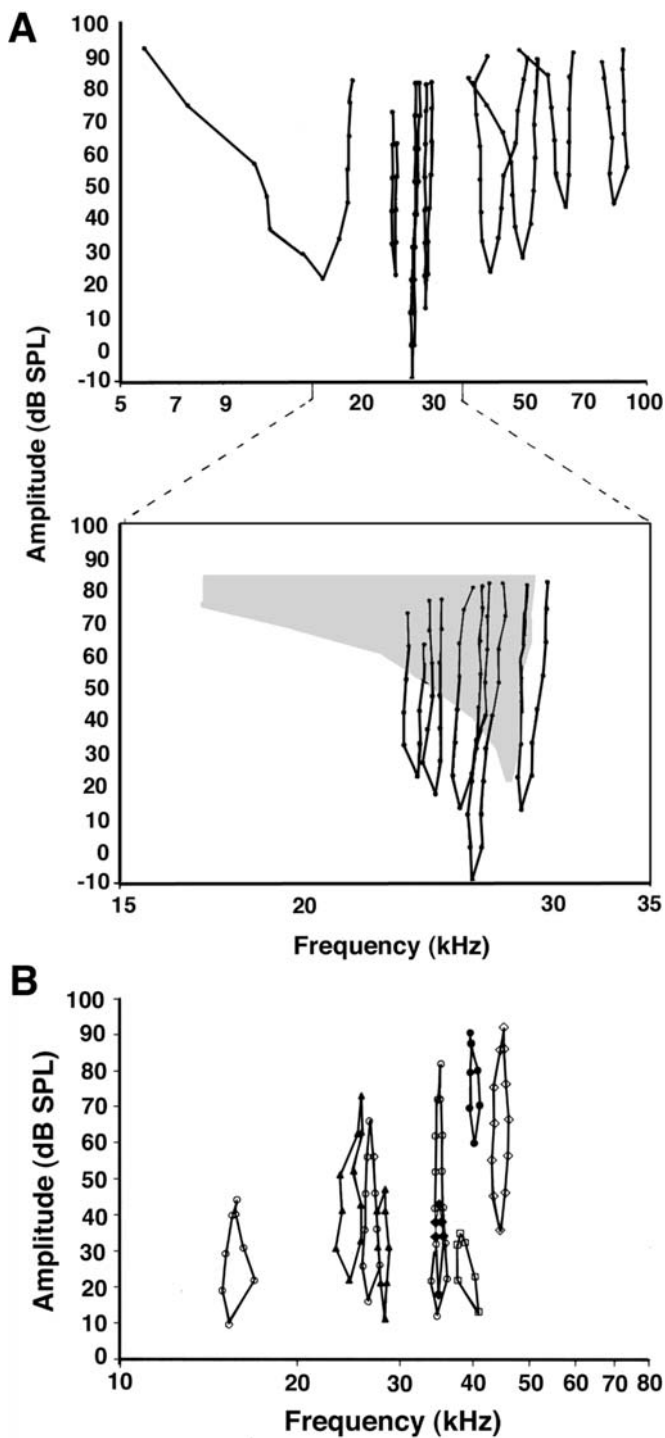


Figure 17.10. (A) Response areas in *Eptesicus* IC. The range between 15 and 35 kHz (lower panel) is expanded to better illustrate narrow, level-tolerant frequency response areas. Gray shading, a V-shaped frequency response area for comparison. (B) Neurons with upper thresholds and closed frequency response areas. (From Casseday and Covey 1992.)

5. RESPONSE PROPERTIES OF INFERIOR COLLICULUS NEURONS

In all vertebrates the auditory midbrain receives excitatory, inhibitory, and modulatory input from many sources, arranged as overlapping and intersecting gradients. The inputs terminate in various ways on different neuronal types, each with specific membrane properties, creating heterogeneous response properties (see Chapters 2, 10, and 11). It is often possible to relate neuronal responses to sound attributes such as frequency, amplitude, duration, the rate and/or depth of modulation in both amplitude and frequency, and the interval separating sounds. It has been possible to localize specialized response properties to particular IC regions in both bats and birds.

5.1. FUNCTIONAL CHARACTERISTICS OF BAT INFERIOR COLLICULUS CELLS

5.1.1. Frequency and Amplitude Tuning

Single neurons have many types of frequency response areas, including simple V-shaped tuning curves, multi-peaked areas, closed response areas with lower and upper thresholds, and narrow, level-tolerant “filter” types (Casseday and Covey 1992). (See Fig. 17.10.)

In CF-FM bats with cochlear specializations, frequency response areas of “foveal” neurons are largely determined by cochlear mechanical properties (Suga et al. 1975). These neurons typically respond to a 1- to 2-kHz frequency band, with their tuning breadth constant across amplitude. This “filter-type” response area (Fig. 17.10A) contrasts with the V-shaped frequency response areas of neurons tuned to other frequencies.

Although *Eptesicus* has no cochlear specializations, it too has neurons with filter-type frequency response areas, tuned to a 1- to 2-kHz band near the bat’s quasi-CF calls. Filter-type response areas have not been found below the level of the IC in *Eptesicus* (Haplea et al. 1994). Frequency tuning can be narrowed considerably by synaptic inhibition (Yang et al. 1992; Pollak and Park 1993; Fuzessery and Hall 1996). In FM bats without cochlear specializations, inhibition produces the same filter property that is mechanically derived in other species, an example of convergent evolution. Perhaps narrow, level-tolerant frequency response areas are essential for processing CF or quasi-CF calls and echoes.

Many IC neurons have nonmonotonic rate-level functions: as amplitude grows their activity increases up to a point and declines or saturates (Suga 1968; Casseday and Covey 1992). Because neurons with nonmonotonic rate-level functions have a variety of “best amplitudes” (Fig. 17.10B), some respond only to the loud echolocation call, others only to the faint echoes. Amplitude tuning

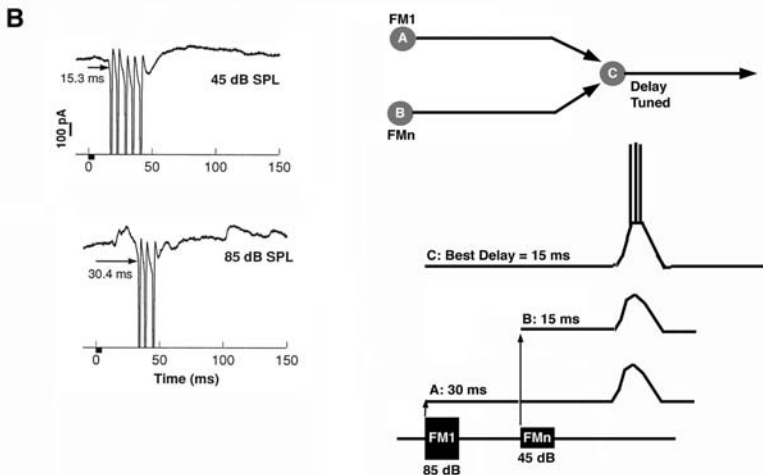
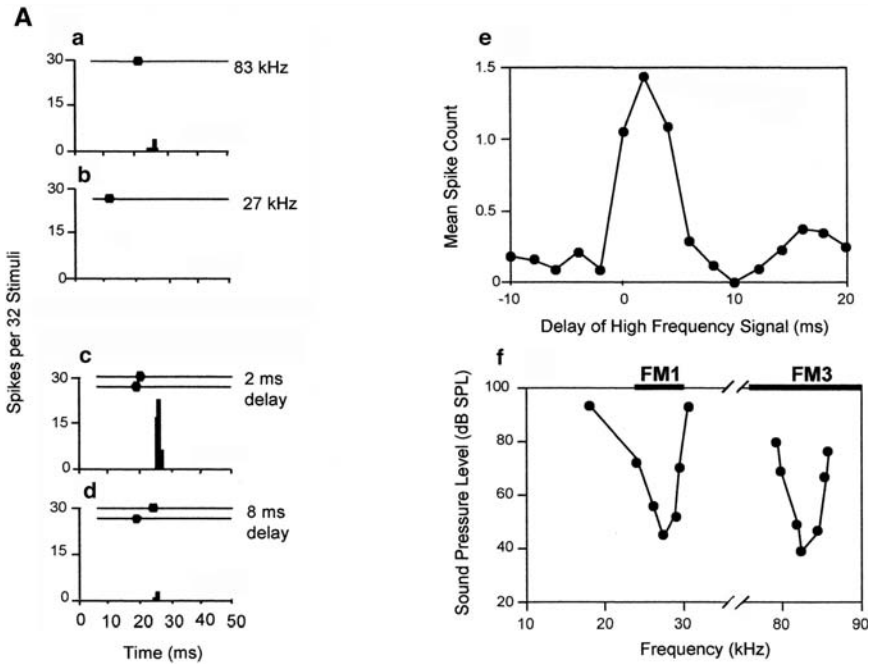


Figure 17.11. (A) A combination-sensitive delay tuned neuron in *Pteronotus* IC. *a, b*: Responses to 83-kHz and 27-kHz tones alone. *c, d*: Responses when the 27-kHz tone was followed by the 83-kHz tone at two different interstimulus intervals (ISI). *e*: Mean spikes/tone pair as a function of ISI. *f*: The neuron had one excitatory response area near the fundamental (first) harmonic of the echolocation call and another near the third harmonic. (From Portfors and Wenstrup 1999.) (B) Paradoxical latency shift (PLS; left) in *Eptesicus* IC. Latency to an 85-dB tone was almost 15 ms longer than to a 45-dB tone. Diagram (top right) of a circuit that could produce delay-tuning if neurons A and B have a similar PLS. Because FM1 is loud in the emitted call, neuron A's latency would be 30 ms, while B's response to the attenuated nth echo harmonic would be 15 ms. The combined EPSP evoked by A in response to the call and in B in response to the echo would be maximal at neuron C when there is a 15-msec echo delay.

might provide a mechanism for segregating responses to calls and echoes for parallel processing (Rübsamen et al. 1988).

5.1.2. Combination Sensitivity and Delay-Tuning

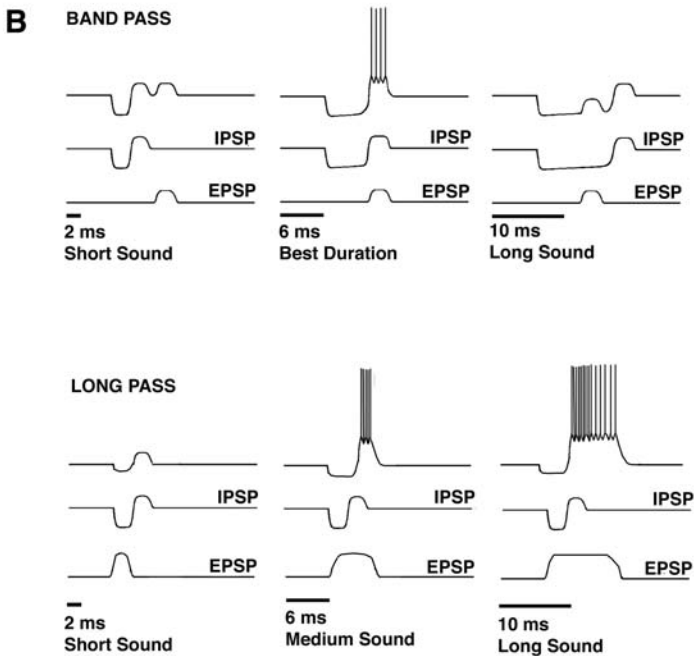
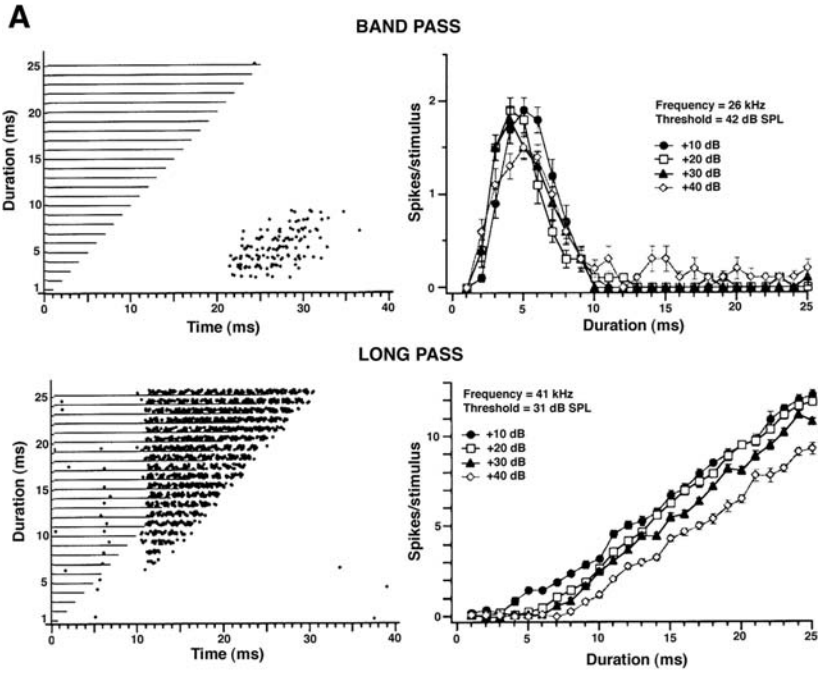
All bat species have IC neurons with multi-peaked frequency response areas (Portfors and Wenstrup 2002). Many neurons are facilitated by combinations of sounds at specific frequencies, with the response to both tones significantly larger than the sum of either alone (Fig. 17.11A). Such facilitation is combination sensitivity and was first described in the intercollicular area of *Eptesicus* (Feng et al. 1978) but is common in the auditory cortex (AC) (Suga et al. 1979; O'Neill and Suga 1979), thalamus (Olsen and Suga 1991), and IC (Mittmann and Wenstrup 1995; Dear and Suga 1995; Portfors and Wenstrup 2001). In one form of combination sensitivity, two frequencies facilitate each other only when presented sequentially in a specific temporal relationship (Fig. 17.11A). Because facilitation depends on the interstimulus interval, such neurons are "delay tuned."

In *Pteronotus*, delay-tuned neurons require tones of different frequencies to produce facilitation. The initial stimulus must often be within the frequency range of the first (fundamental) harmonic of the FM portion of the echolocation call (FM1). Because the FM1 amplitude is weak relative to that of the other harmonics, it likely will be below threshold in the echoes. The second stimulus must be within the frequency range of the second, third, or fourth FM harmonic (FM2, FM3, or FM4, collectively designated FMn). In *Pteronotus* AC, neurons tuned to different delays between FM1 and FMn are organized systematically (O'Neill and Suga 1982). However, there is no topographic organization of best delays in the IC, nor any systematic relation between response latency and best delay (Portfors and Wenstrup 2001), suggesting that "mapping" of best delay occurs at the AC.

The delay between the emitted call and its echo is proportional to the distance of the reflective object; the best delays in IC, MGB, and AC neurons correspond to the range of values for realistic object distances. Therefore, combination-sensitive delay-tuned neurons may be a specialization for echolocation. Other combination-sensitive delay-tuned neurons are facilitated by sounds in frequency combinations that are harmonically unrelated and/or that are outside the frequency range of echolocation calls (Leroy and Wenstrup 2000), and may be involved in processing communication sounds.

5.2. MECHANISM FOR DELAY-TUNING

Most work on delay-tuning mechanisms has used *Pteronotus*. One hypothesis that flowed from Jeffress's work (1948) was that delay-tuned neurons act as coincidence detectors, although on a much longer time scale than for sound localization. In this model, the delay-tuned neuron receives delayed excitatory input from FM1 neurons and rapid excitatory input from FMn-tuned neurons, firing only when the FM1-FMn delay compensates for the delay in the FM1



pathway, making the inputs coincident. Delay-tuned neurons respond to certain interpulse intervals with a peak “best delay” (O’Neill and Suga 1982), consistent with partial coincidence of excitatory postsynaptic potentials (EPSPs) at some delays and complete coincidence at the peak of the delay-tuning function. However, glycine antagonists abolish delay-tuning in IC neurons that show facilitation (Wenstrup and Leroy 2001), suggesting that inhibition is involved.

One mechanism might be paradoxical latency shift (PLS) (Sullivan 1982), presumably using neural inhibition. For most cells, latency decreases with increasing sound level, but paradoxical latency neurons respond with longer latencies as sound level grows (Fig. 17.11B). Some *Eptesicus* IC neurons show PLS due to increasing strength and duration of inhibition at higher sound levels (Covey et al. 1996). PLS cells would respond to the loud echolocation call with a longer latency than to the faint echo. The amount of latency shift would determine best delay (Fig. 17.11B). Since the latency shift varies according to sound level, this may be a mechanism for PLS neurons that changes best delay as a function of amplitude, and it might explain why blocking glycinergic inhibition abolishes delay-tuning.

5.3. DURATION TUNING

Duration sensitive neurons (Fig. 17.12A) are common in the bat IC. Duration tuned neurons typically have a peak response at some best duration (Pinheiro et al. 1991; Casseday et al. 1994; Ehrlich et al. 1997; Fuzessery and Hall 1999) with best durations near the range of call durations used by bats while echolocating. In *Eptesicus* one third of IC cells are duration tuned. They are mainly in the caudal half of the IC, and have not been found below the IC. The underlying mechanisms involve convergence of excitatory and inhibitory inputs with different latencies and discharge patterns (Casseday et al. 1994, 2000). Blocking inhibition abolishes duration tuning in nearly all such neurons (Casseday et al. 2000) and in a subset of these cells in *Antrozous* (Fuzessery and Hall 1999).

Figure 17.12. (A) Duration sensitive *Eptesicus* IC cells. Composite dot rasters (*left*) from band-pass (*top*) and long-pass (*bottom*) cells with 10 presentations/duration (*horizontal bars*). Spike count vs. duration (*right*) at several sound levels. Duration sensitivity is level tolerant. (From Faure et al. 2003.) (B) Model for duration sensitivity created by the interaction of excitatory and inhibitory inputs with different time courses and latencies. The band-pass neuron (*top traces*) receives a transient subthreshold EPSP with a 10-ms onset latency and a sustained 4-ms latency IPSP, followed by an excitatory rebound. The neuron does not reach threshold unless sound duration is such that the EPSP coincides with the rebound from inhibition. Best duration reflects latency differences between the EPSP and IPSP. A short-pass neuron would result when the difference is very small. The long-pass neuron (*bottom traces*) receives a sustained EPSP with a 5-ms latency which, alone, is suprathreshold. The neuron also receives a transient IPSP with similar latency. At short durations, the EPSP is cancelled by the IPSP, but at longer durations the later part of the EPSP is unaffected and elicits a response.

All *Eptesicus* duration tuned neurons receive inhibition for the stimulus duration and have a shorter latency than for excitation. At the end of the inhibitory period, corresponding to stimulus offset, an excitatory rebound occurs that, alone, is subthreshold (Covey et al. 1996). If the sound duration allows the rebound to coincide with the transient excitation evoked by sound onset, facilitation occurs and the neuron responds (Fig. 17.12B). Thus, the cell's best duration reflects the difference between the latencies of inhibition and excitation. Consistent with this model, duration tuned neurons respond at the stimulus offset.

Long-pass neurons' duration sensitivity results when a neuron receives sustained excitation and transient inhibition at about the same latency (Faure et al. 2003). At short durations the excitation is sufficiently brief to be nullified by inhibition, and at longer durations it outlasts the inhibition and drives the neuron (Fig. 17.12B).

5.4. TUNING TO FREQUENCY AND AMPLITUDE MODULATIONS

All bats use FM sweeps in their echolocation call repertoire. Some IC neurons respond only to frequency sweeps and many of these are selective for the direction of frequency change (Suga 1969; Fuzessery 1994). IC neurons preferring either downward or upward FM (Fuzessery 1994) may process communication calls and echolocation signals.

For bats that use CF or quasi-CF calls, insect wing beats can produce periodic amplitude modulations and Doppler shifts in the echo frequency. Echoes of FM calls may contain significant amplitude modulations from interference patterns of reflections from multiple surfaces. Sinusoidal amplitude modulations (SAM) and sinusoidal frequency modulations (SFM) are artificial stimuli that mimic these patterns of amplitude and frequency change. Half of IC neurons respond to sinusoidally modulated stimuli with periodic, phase-locked discharges (Schuller 1979; Casseday et al. 1997). Some *Rhinolophus* foveal cells respond to SAM of as little as 3% depth and to SFMs with modulation depths as small as 0.025%.

IC neurons' discharge patterns in response to pure tones are related to their responses to modulated stimuli. *Pteronotus* ON-OFF neurons are unresponsive to SAM (Lesser et al. 1990) and receive an initial inhibitory input with a shorter latency than that of excitation. When presented with pairs of tones separated by a short interval, both populations experience a phenomenon similar to backward masking. These cells do not code periodic amplitude modulations because the response to the earlier stimulus is suppressed by the short-latency inhibition evoked by the second stimulus. Because many IC neurons receive inhibition before excitation (Covey et al. 1996), backward masking may set the upper limit for modulation rate. IC neurons respond to SAM only up to 100 to 200 Hz (Reimer 1987) even though the presynaptic cells respond to higher modulation rates. Because blocking GABAergic and glycinergic inhibition (Burger and Polak 1998) has little effect on SAM tuning, intrinsic properties may be more important than inhibition for tuning to AM rate.

Some *Eptesicus* IC neurons respond only to SFM (Casseday et al. 1997), requiring several cycles to become primed. Perhaps each cycle of frequency modulation elicits an inhibitory event followed by a subthreshold excitatory event. If the modulation rate for the excitatory rebound that follows the inhibition from one half-cycle coincides with the excitation evoked by the next half-cycle, the neuron reaches threshold and fires. Blocking inhibition broadens SFM tuning (Koch and Grothe 1998), suggesting that neural inhibition may contribute to tuning to SFM rate.

5.5. ROLE OF THE BAT INFERIOR COLLICULUS IN BINAURAL HEARING AND SOUND LOCALIZATION

Bat IC neurons, like those of other mammals, have many binaural interaction patterns, but there is no evidence of a space map like that in the barn owl. Because most mammals move their eyes, the relationship between the visual and auditory fields is variable. Many mammals also have mobile pinnae, complicating the relation between the head and the auditory field.

Many bats have large, complex, and mobile pinnae that are highly directional and accentuate ILDs. They also produce characteristic spectral patterns that could aid in localization in both azimuth and elevation (Fuzessery and Pollak 1984; Wotton et al. 1995). The response patterns of all IC neurons likely reflect the pinna's characteristics, imparting some spatial tuning, especially at sound levels just above threshold (Grothe et al. 1996).

IC binaural properties are not simply inherited from LSO or MSO, but instead reflect integration of excitatory and inhibitory synaptic input. Both GABAergic and glycinergic inhibition actively shapes binaural response properties (Vater et al. 1992a; Park and Pollak 1993, 1994; Klug et al. 1995; Pollak 1997). Some cells experience inhibition when sound is presented at one ear and excitation when it is presented at the other, and the latency and time course of each is different (Covey et al. 1996). Because binaural processing does not construct a fixed auditory space representation, it may have other roles such as enhancing the detection of signals in noise, reducing echo clutter, or coding sound source motion.

Specific binaural subclasses are excited by inputs from the contralateral ear and inhibited by the ipsilateral ear (EI) or excited by inputs from the contralateral and ipsilateral ear (EE). Cells representing these classes are segregated spatially and there are progressive shifts in the excitatory–inhibitory balance of inputs from the ears that form gradients across the IC. When ILD function 50% points (or cutoffs) are measured across an isofrequency contour, the points create a gradient in which ILD functions extend into ipsilateral space (Wenstrup et al. 1986). However, spatial receptive field (RF) properties interact with sound amplitude, frequency spectrum, modulation pattern, sound source movement, and other stimulus aspects (Grothe et al. 1996), so individual neurons, or even populations, are unlikely sources for unambiguous spatial information.

5.6. INTERACTIVE PROCESSING

Convergent inputs differentially tuned to many sound parameters suggest that neural responses are interactive. Stimulus amplitude or spectrotemporal changes affect spatial RF size and shape (Grothe et al. 1996; Wu and Jen 1996) and stimulus repetition rate can influence latency, rate-level functions, thresholds, frequency tuning, and duration tuning (Jen and Chen 1998; Jen et al. 2001; Zhou and Jen 2001). Some interactions depend on GABAergic inhibition (Jen et al. 2002). The sound-evoked sequence of synaptic currents can exceed the sound's duration, imposing context-dependent alterations of the subsequent responses (Covey et al. 1996).

5.7. PLASTICITY OF RESPONSES

IC neural response properties show long-term plastic changes caused by corticocollicular input (Suga et al. 2002; Suga and Ma 2003). Tuning changes can reflect behavioral conditioning (Gao and Suga 1998) or experimental manipulations of AC, including electrical stimulation (Yan and Suga 1996) or inactivation (Yan and Suga 1999). Effects on frequency tuning (Zhang et al. 1997), interstimulus interval (Yan and Suga 1996), and sound duration (Ma and Suga 2001) are seen. Conditioned changes in responses require 15 to 30 minutes of stimulation under constant conditions and last for hours (Ji et al. 2001). Cortical manipulations have similar effects on all parameters tested. In *Pteronotus*, AC electrical stimulation in an area where neurons are tuned to a particular parameter value augments IC responses of cells tuned to that parameter value and decreases that of neurons tuned to different values of the same parameter, perhaps enhancing the representation of a common sound.

6. FUNCTIONAL CHARACTERISTICS OF AVIAN MIDBRAIN NEURONS

Save for barn owls and songbirds, we do not know what acoustic properties are behaviorally salient to birds (Konishi 1985). Nevertheless, IC responses in barn owl, chicken, and zebra finch IC are similar, and principles learned from studies of the barn owl IC may apply to other birds (Knudsen et al. 1979).

Barn owls can localize sound precisely, and their midbrain responses are dominated by binaural computations subserving localization (Keller and Takahashi 1996; Konishi 2000). Their IC neurons are EE or EI (Moiseff and Konishi 1981) and sensitive to changes in ILD and ITD. Similarly, most chicken neurons are binaural, 46% being EI, 21% EE, 8% II (inhibited by either ear), and only 17% are monaural (Coles and Aitkin 1979).

Physiological properties are subdivision specific. The ICCc contains ITD-sensitive neurons and projects to the contralateral lateral shell, where ITD in-

formation is combined with ILD information (Fig. 17.13; Coles and Aitkin 1979; Takahashi et al. 1987a; Wagner et al. 1987; Volman and Konishi 1989; Spezio and Takahashi 2003). Thus, the progression from ICC to ICX is associated with the abstraction of stimulus features required to construct the ICX auditory space map (Mazer 1997).

6.1. INTERAURAL TIME DIFFERENCE TUNING

ITD is the principal cue for auditory azimuth (Moiseff and Konishi 1981) and is computed in two stages: first, brain stem NL neurons act as coincidence detectors to encode interaural phase difference, firing maximally when simultaneously receiving inputs from both ears (Carr and Konishi 1990; Peña and Konishi 2001). At this stage, ambiguities exist about the correspondence between the NL response and the actual ITD in auditory space. The second stage of ITD computation occurs in the IC, where across-frequency integration filters phase-ambiguous side peaks, creating neurons coding the true ITD (Takahashi and Konishi 1986; Peña and Konishi, 2000).

The ICCc receives NL input and contains sharply frequency-tuned ITD sensitive neurons with primary-like responses (Fig. 17.13; Coles and Aitkin 1979; Wagner et al. 1987). In the ICCc one ITD activates a neural array tuned to many different frequencies (Fig. 17.13F; Wagner et al. 1987). This array code is transformed into unambiguous space-specific neuron responses as follows. Each array projects to ITD- and ILD-sensitive neurons in the contralateral lateral shell (ICCLs), which project to space-specific neurons in the contralateral ICX, endowing them with ITD selectivity and therefore azimuth coding (Takahashi and Konishi 1986; Mazer 1997; Peña and Konishi 2000).

6.2. TUNING TO LEVEL AND INTERAURAL LEVEL DIFFERENCE PROCESSING

Less is known about ILD processing. In the barn owl, the vertical asymmetry in ear directionality makes ILD a cue for the vertical target axis at high frequencies. Level is encoded by CN neurons, most having monotonic rate level functions (Köppl and Carr 2003). ILD sensitivity first emerges in the dorsal nucleus of the lateral lemniscus, posterior part (LLDp) whose neurons are excited by contralateral stimulation and inhibited by ipsilateral stimulation (Takahashi and Keller 1992; Takahashi et al. 1995) and are EI cells coding ILD (Manley et al. 1988; Mogdans and Knudsen 1994). LLDp therefore is analogous to LSO (Tsuchitani 1977; Takahashi et al. 1995). LLDp projects bilaterally to the ICCLs, endowing these cells with ILD sensitivity (Adolphs 1993).

LLDp neurons do not unambiguously encode ILD. Although they prefer sound at the contralateral ear, they are also sensitive to changes in average binaural level. ILD tuning gradually emerges in the ICCLs (Mazer 1998). Response latencies are about 5 ms near the central core, and >10 ms at the ICX

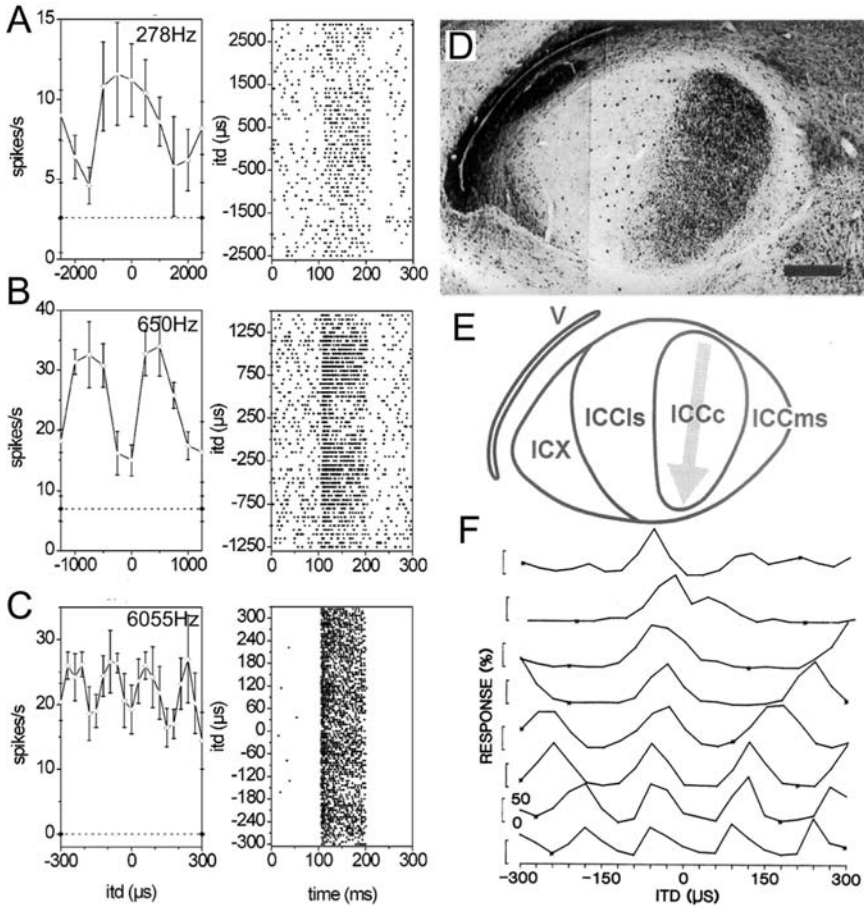


Figure 17.13. (A) ITD tuning curves in the barn owl ICCc. *Left*, ITD tuning curves; *right*, raster plots. Positive ITDs are right-ear leading. Tuning curves (*a*, *b*, *d*) from low- and high-frequency neurons. (B) The stimulus is an 800-Hz tone; all others are broadband noise. Note the cyclical tuning, even in response to noise stimuli, and the inhibition of spontaneous activity at stimulus termination. (D, E) Calretinin immunohistochemistry labels the ICCc; *arrow*, best frequency axis. (F) The ensemble code for ITD in the ICC. The array is sensitive to interaural phase differences, but each response shows phase ambiguity. (Modified from Wagner et al. 1987, 2002; Kubke et al. 1999.)

border. Frequency tuning widths broaden with increasing lateral position, while ITD and ILD tuning widths sharpen. Almost all ICCls neurons are sensitive to both time and intensity cues (Mazer 1997).

Unlike the ITD coding array in the ICCc, a topographical representation of ILD is never observed in the ICCls (Mazer 1998). Recordings from the space specific neurons show instead that ILD varies as a function of frequency in a

complex manner for any given location (Fig. 17.14A). In ICX, ILD-alone RFs are generally horizontal swaths of activity at the elevation of the cell's normal spatial RF (Fig. 17.14A). An ITD-alone RF forms a vertical swath at the azimuth of the cell's normal RF, which thus lies at the intersection of the ITD- and ILD-alone RFs (Euston and Takahashi 2002). ILD sensitive neurons in the chicken are EI and encode a 10- to 15-dB range (Coles and Aitkin 1979), with responses like those in the barn owl.

6.3. *THE MAP OF AUDITORY SPACE IN THE EXTERNAL NUCLEUS*

The ICX space-specific neurons respond to sound only from a particular spatial locus and, when spontaneously active, are inhibited by stimulation of either ear (II) (Fig. 17.15; Knudsen and Konishi 1978; Knudsen and Knudsen 1983; Takahashi and Konishi 1986) and they are selective for combinations of ITD and ILD. Driven by noise, they do not show phase ambiguity, and thus differ from the ICCc ITD sensitive cells that provide their input (Peña and Konishi 2000). The phase-unambiguous response of space-specific neurons has been explained as follows. They receive inputs via the ICCIs from many ICCc isofrequency laminae (Knudsen 1983), presumably from the ITD-specific arrays (Wagner et al. 1987). These inputs interact at the postsynaptic cell: peaks signaling the correct ITD superimpose and add, while secondary, ambiguous peaks cancel by interacting with inhibitory sidebands from other or ambiguous frequencies (Takahashi and Konishi 1986; Keller and Takahashi 1996, 2000). The inhibitory interactions between different frequency channels may originate from GABAergic ICX neurons (Fujita and Konishi 1991).

ICX neurons act like analog AND gates for ITD and ILD, such that the two inputs are multiplied (Fig. 17.14B–E). Multiplication of separate postsynaptic potentials (PSPs) tuned to ITD and ILD, rather than an additive process, explains their subthreshold responses to ITD-ILD pairs. Comparing subthreshold PSPs and spike output for the same ICX neurons show that RFs measured in PSPs exceed those measured in spikes in both ITD and ILD dimensions. Thus, a spike threshold mechanism mediates formation of the restricted space specific RF, the stimulus-induced first spike having a lower threshold than subsequent or spontaneous spikes (Peña and Konishi 2001).

The spatially restricted ICX RFs are still much larger than the minimum detectable change in sound source location, which can be 3°. However, changes in neuronal activity across the space map show that most neurons can reliably signal source location changes smaller than the behavioral threshold. Each source is represented in the space map by a focus of activity in a neural population, and source displacement changes their activity pattern (Takahashi et al. 2003). This map of contralateral auditory space projects topographically to the optic tectum (OT), whose visual and auditory space maps are in register (Knudsen and Knudsen 1983). OT activity directs the owl's rapid head movements to auditory and visual stimuli (du Lac and Knudsen 1990).

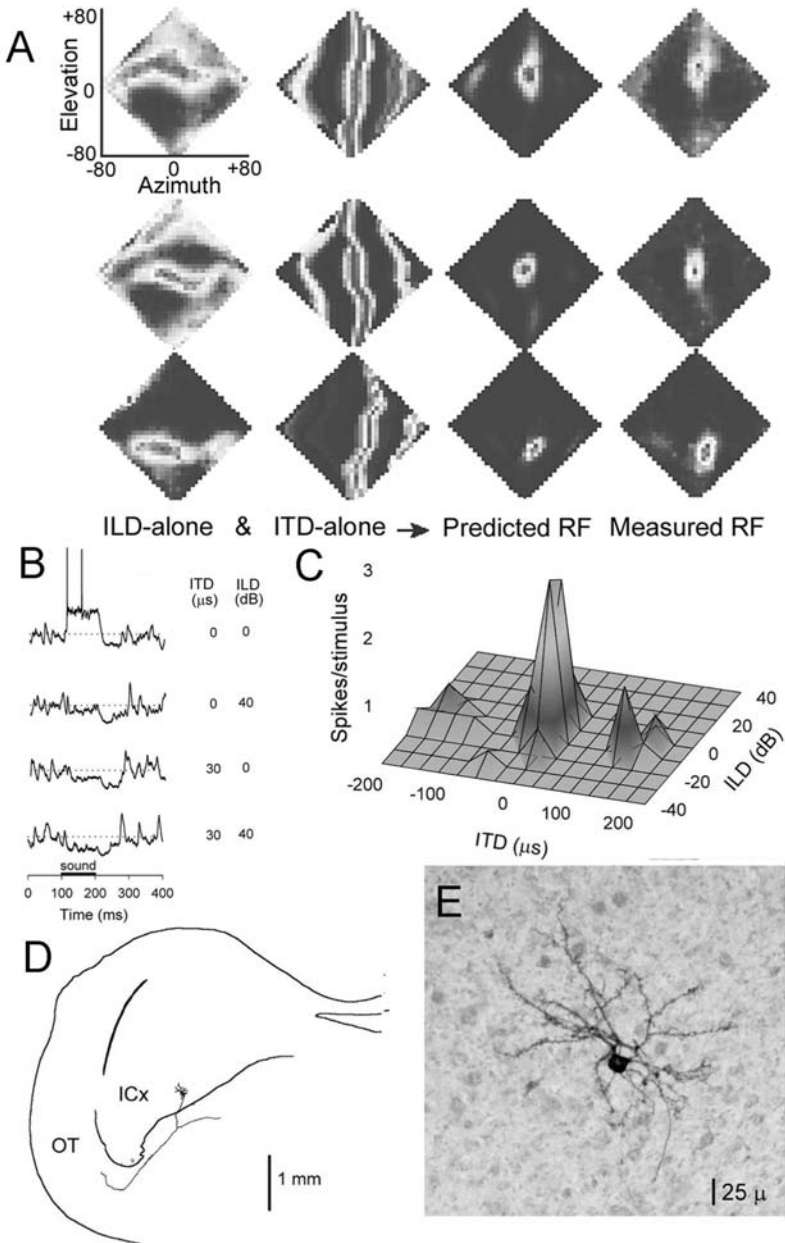


Figure 17.14. Formation of space-specific responses in the barn owl ICX. (A) ITD and ILD contributions to the spatial RF of an ICX cell. Diamond, spikes (gray) evoked by a source at frontal hemisphere loci. *First column*: ILD-alone RFs for three cells obtained by filtering broadband noise with HRTFs altered to present the ILD spectra for each spatial location while holding the ITD constant at a cell's preferred value. *Second column*:

6.4. THE ROLE OF EXPERIENCE IN FORMATION OF THE SPACE MAP

The auditory space map has become a paradigm for studies of experience-dependent plasticity (Knudsen 2002). Manipulating sensory experience reorganizes ICX in a manner congruent with behavioral learning, as accurate auditory orienting behavior is a measure for adaptive adjustment in sound localization after peripheral changes in sensory experience such as disrupting auditory cue values for spatial loci by ear plugging (Knudsen et al. 1984; Brainard and Knudsen 1995; Knudsen 1999). Owls with an earplug first err toward the open ear, then recover. On earplug removal, their orienting errors are in the opposite direction, and these resolve with experience. A second manipulation alters visual and auditory correspondence with prismatic spectacles that displace the visual field (Brainard and Knudsen 1998). Such owls learn new associations between auditory and visual cues to recalibrate both worlds.

Learning changes forebrain and midbrain neuron tuning to sound localization cues. In the midbrain space map, the assay for plasticity is precise and can be quantified for each neuron (Fig. 17.15; Knudsen 1982). Adaptive changes are centered in the ICX and depend on changes in axonal projections and adjustments in synaptic strength (Knudsen 2002; Nieder et al. 2003). In young owls with either earplugs or prismatic displacement, ICX tuning to sound localization cues alters adaptively to coordinate the auditory and the visual RFs (Fig. 17.15; Mogdans and Knudsen 1994). Gradually, these new responses strengthen, while those to the prior ITD range disappear. These changes are correlated with axonal remodeling of the topographic projection from the ICC to the ICX. Prism experience appears to induce the formation of modified circuitry in the ICX at least in part through axonal sprouting and synaptogenesis. Normal circuitry also persists, showing that alternative plastic and normal circuits coexist in this network.

Both *N*-methyl-D-aspartate (NMDA) and GABA_A receptor changes are implicated in plasticity. NMDA receptors regulate expression of newly learned responses (Feldman and Knudsen 1998). In an ICX expressing a maximally shifted

Figure 17.14. *Continued*

the ITD-alone RFs. *Third column*: combining the plots in these columns yields the predicted spatial RFs. *Fourth column*: spatial RFs measured directly from the cell. Negative azimuths and elevations denote loci on the left of the midline and below eye level, respectively. (Modified from Takahashi et al. 2003.) **(B)** Space specific neuron showing PSPs to different ITD–ILD pairs. *Dotted lines*, mean resting potential. **(C)** Spiking responses of the same neuron to different ITD–ILD pairs. The large peak is the excitatory center and the flat area around it is the inhibitory surround (compare **B**, **C**). Negative (–) ITD and negative (–) ILD mean, respectively, sound in ipsilateral ear leading and louder. **(D)** An ICX neuron and its axon projecting to the OT. **(E)** The same neuron labeled with neurobiotin. (From Peña and Konishi 2001.)

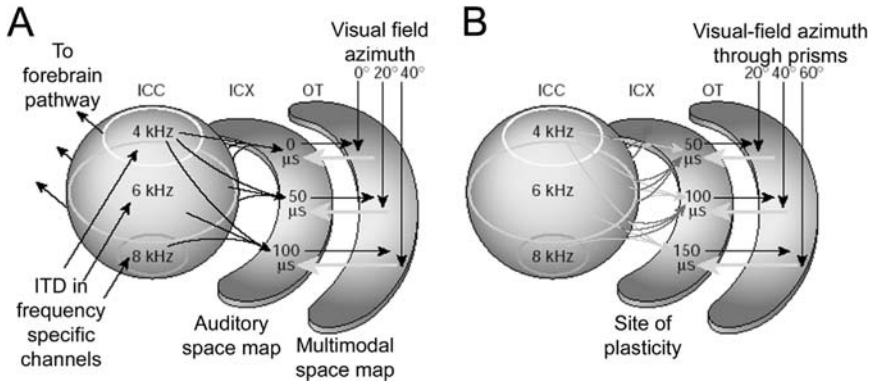


Figure 17.15. The auditory space map in the ICX before (A) and after (B) shifts produced by early prism experience. (A) The ICC–ICX (*black arrows*) projection conveys ITD and other information and converges across frequency channels, creating spatially restricted auditory RFs and a space map. The auditory and visual maps of space merge in OT and receives a reciprocal instructive signal from it. (B) The schematic representation of the anatomical change (*dark arrows*) in the ICC–ICX projection resulting from early prism experience. For each axis of prismatic displacement, an abnormal rostralward projection of ICC axons (*dark gray arrows*) appears on one side of the brain and a caudalward projection appears contralaterally (data not shown), although the normal projection persists (*light gray arrows*). (Modified from Knudsen 2002.)

ITD map, focal blockade of GABA elicited the immediate appearance of normal responses. Thus, in a shifted-ITD map, synapses that support normal responses remain patent and coexist with synapses that support learned responses, but responses to the normal synapses are selectively nullified by GABAergic inhibition (Zheng and Knudsen 1999).

Changes in the ICX auditory space map are directed by a topographic map of visual space whose dominance is plausible since the pathway's primary function is to trigger gaze towards auditory targets (Knudsen et al. 1993; Wagner 1993). The power and precision of the visual instructive signal is shown when a small lesion in the tectum eliminates adaptive adjustments (Hyde and Knudsen 2002).

7. COMPARING BIRDS AND BATS

The auditory midbrain structures of birds and bats are probably homologous, and serve many similar purposes. The IC integrates information converging on it from many parallel pathways that will ultimately contribute to sound source localization and decoding of the auditory signals. The IC is an important source of output to motor pathways for orientation, vocalization, and other behaviors. It is part of a massive system that extends to the forebrain, and it may participate

in adaptive changes from learning and peripheral modifications. However, the evolutionary paths of birds and bats diverged so long ago that many of the substrates through which these tasks are accomplished are very different. The avian cochlea, central auditory system, and forebrain are organized differently from those of mammals so that the patterns of connections differ considerably between the two groups.

Midbrain organization is more hierarchical in owls, especially with regard to the emergence of an invariant map of auditory space in the different IC subdivisions. The barn owl midbrain is dominated by binaural processing and may have more in common with mammals that do not echolocate. Finally, the streams of processing for sound location and temporal patterns are more sharply segregated in owls. Future work should reveal whether birds and bats share some of the same neural circuits and cellular mechanisms for information processing despite the fact that many structures and pathways are different.

Abbreviations

AVCN	anteroventral cochlear nucleus
CF	constant-frequency
CN	cochlear nucleus
DCN	dorsal cochlear nucleus
DLL	dorsal nucleus of the lateral lemniscus
EE	neuron excited by contralateral and ipsilateral sound
EI	neuron excited by contralateral sound and inhibited by ipsilateral sound
EPSP	excitatory postsynaptic potential
FM	frequency-modulated
GABA	γ -aminobutyric acid
GC	tectal gray
IC	inferior colliculus
ICC	central nucleus of the inferior colliculus
ICCc	central core of the central nucleus of the inferior colliculus
ICCl _s	lateral shell of the central core of the inferior colliculus
ICCm _s	medial shell of the central core of the inferior colliculus
ICX	external nucleus of the central core of the inferior colliculus
III	oculomotor nucleus
ILD	interaural level difference
ILL	intermediate nucleus of lateral lemniscus
IO	isthmo-optic nucleus
IPSP	inhibitory postsynaptic potential
ITD	interaural time difference
IV	trochlear nucleus
iv	trochlear nerve
LL	lateral lemniscus

LLDp	dorsal nucleus of lateral lemniscus, posterior part
LSO	lateral superior olive
MGB	medial geniculate body
MLd	mesencephalic nucleus, pars dorsalis
MSO	medial superior olive
NA	nucleus angularis
NL	nucleus laminaris
NM	nucleus magnocellularis
NMDA	<i>N</i> -methyl-D-aspartate
PLS	paradoxical latency shift
PVCN	posteroventral cochlear nucleus
RF	receptive field
SAM	sinusoidal amplitude modulation
SFM	sinusoidal frequency modulation
SOC	superior olivary complex
VLL	ventral nucleus of lateral lemniscus
VLLc	columnar nucleus of VLL

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