Chapter 15

Cortical Representation of Auditory Space

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Abbreviations

AAF   anterior auditory field
AI   primary auditory cortex
AII   secondary auditory cortex
AES   anterior ectosylvian sulcus
DZ   dorsal zone
IC   inferior colliculus
ILD   interaural level difference
ITD   interaural time difference
PAF   posterior auditory field
SC   superior colliculus

1 Introduction

It has been known for many years that an intact auditory cortex is necessary for the normal ability of carnivores and primates, including humans, to localize sound sources. As such, the auditory cortex plays an essential part in one of the most important functions of hearing, which is critical to the way in which these species perceive and interact with their environments. For example, the ability to determine the direction of sound-producing objects or events is often used to find potential mates or prey or to avoid and escape from approaching predators. Sound localization also contributes in important ways to the process by which different sound sources are segregated from one another and therefore aids source identification.

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Information about the direction of a sound source is provided in the form of physical cues that are generated by the way in which incoming sounds interact with the head and external ears. These cues comprise differences in the time of sound arrival and amplitude level between the two ears, together with spectral shape cues produced by the filter properties of these structures. In mammals, binaural cues are utilized for localizing sounds within the horizontal plane, with interaural time differences (ITDs) dominating at low frequencies and interaural level differences (ILDs) at high frequencies, whereas spectral cues enable listeners to localize sounds in elevation and to distinguish between front and back (Wightman and Kistler 1993). These acoustical cues are encoded in the patterns of activity in each auditory nerve and then extracted by neurons in specific brainstem nuclei (Yin 2002; Young and Davis 2002). The outputs from these nuclei converge within the inferior colliculus (IC) in the midbrain (Winer and Schreiner 2005), where neurons are typically sensitive to multiple localization cues (Chase and Young 2006). The major output of the IC is toward forebrain targets. In addition to the forebrain projection, however, a pathway to the superior colliculus (SC) within the midbrain gives rise to a point-to-point map of auditory space (King and Palmer 1983; Middlebrooks and Knudsen 1984; King and Hutchings 1987), which, together with visual and somatosensory inputs to this structure, is used to direct orienting movements towards specific spatial locations (King 2005).

The existence of a map of auditory space in the SC indicates that substantial processing of spatial information takes place subcortically. Moreover, certain aspects of auditory spatial perception can, in principle, be accounted for by the tuning properties of neurons in the IC (Shackleton et al. 2003). It could therefore be argued that the process of sound localization is largely complete at the level of the midbrain. Nevertheless, given the impaired localization abilities that result when the auditory cortex is no longer functioning, it is clear that a spatially coded signal must be transmitted to the forebrain to support spatial perception and behavior and likely that further essential processing takes place at the cortical level.

We first review the behavioral consequences of ablating or inactivating particular auditory cortical areas and then consider how well these findings can be reconciled with the spatial sensitivity of neurons in those areas. In particular, we focus on how the location of a sound source is encoded by the firing patterns of cortical neurons and how that information might be decoded. Finally, we examine the possible role of descending corticofugal projections in sound localization and the role of auditory cortex in the plasticity of spatial hearing.

2 Inactivation of Auditory Cortex Induces Sound Localization Deficits

Evidence that an intact auditory cortex is required for normal sound localization behavior has been provided by a number of studies showing that removal of the cortex in one hemisphere in carnivores and primates results in an impaired ability to approach, discriminate or even orient toward sound sources in the contralateral hemifield, whereas localization performance on the ipsilateral side is largely unaffected (e.g., Jenkins and Masterton 1982; Jenkins and Merzenich 1984; Kavanagh and Kelly 1987; Heffner and Heffner 1990; Beitel and Kaas 1993). In fact, a contralateral deficit in localization behavior is the most obvious change observed following unilateral removal of the auditory cortex. If the cortex is ablated bilaterally, cats, dogs, ferrets, and monkeys perform poorly in both lateral hemifields, although they generally still show some ability to distinguish between sound sources located in one hemifield from the other (Neff et al. 1956; Heffner and Masterton 1975; Heffner 1978; Kavanagh and Kelly 1987; Heffner and Heffner 1990; Heffner 1997; Nodal et al. 2010).

Although the magnitude of the reported deficits varies with the size of the lesions and the methods used for measuring localization performance, these studies strongly suggest that the auditory cortex in each hemisphere of these species is primarily responsible for localization behavior in the opposite hemifield, with regions near the midline likely to be represented bilaterally. Although an impaired ability to localize sound is found following restricted lesions focused on the primary auditory cortex (AI), several authors have noted that more profound deficits are observed following lesions that extend beyond AI (Heffner and Masterton 1975; Heffner 1978; Kavanagh and Kelly 1987; Bizley et al. 2007; Nodal et al. 2010). This suggests that other cortical fields contribute further to the processing of spatial information.

The use of aspiration lesions for probing the role of auditory cortex in sound localization and other sound-related behaviors has now largely been superseded by cryogenic (Malhotra et al. 2004, 2008; Malhotra and Lomber 2007; Lomber and Malhotra 2008) or pharmacological inactivation techniques (Smith et al. 2004; Bizley et al. 2007; Nodal et al. 2010), which allow neurons in specific regions of the brain to be silenced reversibly. As expected from the lesion studies, these experiments have shown that unilateral inactivation of AI results in contralateral deficits, whereas bilateral inactivation leads to increased localization errors at all positions tested within the horizontal plane (Malhotra et al. 2004; Smith et al. 2004), as well as a reduced ability to discriminate sound sources located on the midsagittal plane (Bizley et al. 2007) (Fig. 15.1).

The deficits observed following temporary inactivation tend to be smaller than those produced by large cortical lesions, with the animals typically still able to orient toward the side on which the sounds are presented, but unable to localize them as accurately as before the cortex was inactivated. This difference is likely due to a combination of factors. First, removal of the cortex causes neuronal degeneration in brain areas, such as the thalamus, to which the affected cortical area is connected. Second, the temporary inactivation experiments have been aimed at specific cortical fields previously identified using physiological and anatomical criteria. Indeed, cooling studies in cats (Malhotra et al. 2004, 2008; Malhotra and Lomber 2007; Lomber and Malhotra 2008) have shown that, in addition to the well-established effects of silencing AI, deficits in spatial hearing result from inactivation of the posterior auditory field (PAF), anterior ectosylvian sulcus (AES), or dorsal zone (DZ), but not when other areas, such as the secondary auditory cortex (AII) or anterior auditory field (AAF) are targeted (Fig. 15.2). These findings imply that a division of labor may exist within auditory cortex, with different areas responsible for the processing of spatial and non-spatial information. There is no one "space region," however, as multiple auditory cortical fields, each with distinct sources of input (Morel and Imig 1987; Huang and Winer 2000), are necessary for normal localization behavior, with certain areas, particularly PAF and AES, appearing to contribute more than others.

Studies in humans have confirmed that damage to the auditory cortex, which can occur as a result of a stroke or following surgery to remove a tumor, results in impaired sound localization (Zatorre and Penhune 2001; Adriani et al. 2003), as well as raised ITD and ILD discrimination thresholds (Yamada et al. 1996). Difficulties in defining the precise locus of the damage, which varies between individuals both in its extent and in the age at which it occurs, inevitably limit the comparisons that can be drawn with the animal studies. However, in contrast to the contralateral representation of auditory space emphasized in other species, humans appear to show a clear right-hemisphere dominance for sound localization (Zatorre and Penhune 2001). Thus, right-sided lesions in humans often result in bilateral localization deficits, and bilateral localization is sometimes spared following a left-sided lesion.
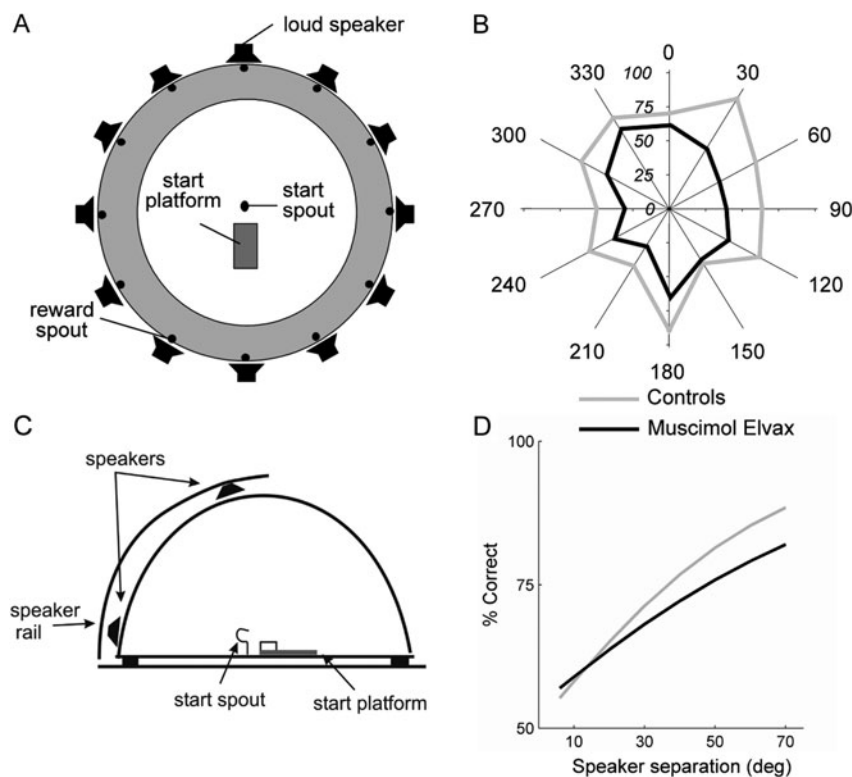
Fig. 15.1 The auditory cortex is needed for normal sound localization. **a** Setup used for measuring localization in the horizontal plane. Ferrets were trained to stand on the start platform and initiate a trial by licking the start spout. Each trial consisted of a broadband noise burst of variable duration and level presented randomly from 1 of 12 speakers positioned at 30° intervals in the horizontal plane. The animals were rewarded for approaching and licking the reward spout associated with the speaker that had been triggered. **b** The polar plot shows the mean percentage scores achieved when localizing 40-ms noise bursts by a group of 4 control ferrets and 4 animals in which A1 had been inactivated bilaterally by placing sheets of a slow-release polymer containing the GABA$_A$ agonist muscimol on the cortex. These animals achieved lower scores than the normal controls at all stimulus angles. From Smith et al. (2004). **c** Setup used for measuring localization in the *vertical* plane. The animals had to discriminate between stimuli presented from one of two speakers positioned in the midsagittal plane. Because it was not possible for the animals to approach the sound source directly, they were rewarded for responding at a reward spout to their right (+90°) when the sound was presented from the upper speaker, and at a spout to their left (–90°) when sound was presented from the lower speaker. **d** Psychometric functions fitted to the data from the same ferrets before (control) and after inactivating AI bilaterally with muscimol-Elvax. In 5 (out of 6) animals contributing to these data, AI inactivation produced a significant drop in performance. From Bizley et al. (2007)

## 3 Representation of Auditory Space in the Cortex

The role established by lesion-behavior studies for the auditory cortex in spatial hearing raises the question of how sound-source location is represented there. This has been addressed by either mapping out the spatial receptive fields of individual cortical neurons or by measuring their sensitivity to acoustic localization cues. As in the behavioral experiments, receptive field mapping studies typically involve recording the spiking activity of the neurons in response to sounds delivered from loudspeakers positioned around the animals' head in the free-field (e.g., Middlebrooks and Pettigrew 1981; Imig et al. 1990; Rajan et al. 1990a, b; Stecker et al. 2005a, b; Woods et al. 2006; Harrington et al. 2008; Werner-Reiss and Groh 2008). Alternatively, stimuli can be presented over headphones in virtual acoustic space, an approach that enables rapid mapping of spatial sensitivity across a broad range of stimulus directions, as well as manipulation of the localization cue values provided (Brugge et al. 1994, 1996; Mrsic-Flogel et al. 2001, 2003, 2005; Las et al. 2008).

3.1 Spatial Receptive Fields in Primary Auditory Cortex

Like the lesion and inactivation studies, early recording experiments focused on AI, while more recent studies have explored the spatial sensitivity of neurons in other cortical areas. We first review the general properties of and acoustical basis for the spatial receptive fields in the primary auditory cortex, which have been determined by recording neuronal responses from both anesthetized and awake animals, and

Fig. 15.2 Localization responses to sounds presented in the frontal hemifield before and after (*i*) and during (*ii*) unilateral cooling deactivation of 6 areas of auditory cortex in the cat: AI (**a**), PAF (**b**), AAF (**c**), AII (**d**), VPAF (**e**), and AES (**f**). The length of each *radial line* indicates the mean percentage correct score for that sound direction. The site and extent of deactivation are shown below each plot by the *black regions* on the medial and lateral views of the cat brain. Inactivation of AI, PAF, and AES each resulted in a contralateral, but not an ipsilateral, localization deficit. Adapted from Malhotra et al. (2004)
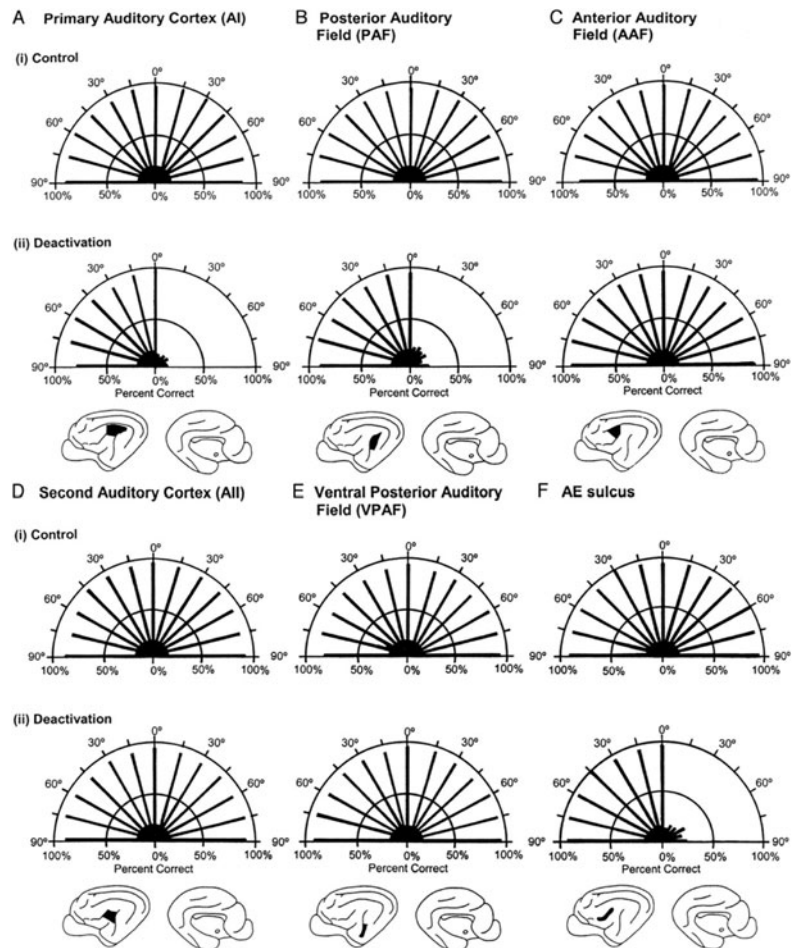
then, in the next section, consider the extent to which these properties vary among different cortical areas.

Cortical receptive fields vary in size, from a minority of neurons that show a clear preference for restricted regions of space to those that respond throughout an entire hemifield or beyond. Generally, receptive fields expand with increasing sound level and also vary in size according to the bandwidth of the stimulus and with other properties of the neuron in question. In keeping with the behavioral deficits produced by unilateral lesions or inactivation, most cortical neurons respond best to sounds presented on the contralateral side of the animal, although some prefer sound sources near the frontal midline or on the ipsilateral side (Fig. 15.3).

The differences in spatial receptive field properties among cortical neurons can be attributed to their tuning to monaural and binaural localization cues. As in subcortical nuclei, low-frequency cortical neurons are sensitive to ITDs (Malone et al. 2002; Scott et al. 2009), whereas high-frequency neurons rely more on ILDs (Imig and Adrian 1977; Middlebrooks et al. 1980; Irvine et al. 1996; Rutkowski et al. 2000; Zhang et al. 2004; Campbell et al. 2006). In both cats (Irvine et al. 1996; Zhang et al. 2004) and ferrets (Campbell

et al. 2006), ILD sensitivity ranges from a minority of neurons showing ipsilateral dominance or tuning to values close to zero, corresponding to sound sources located in front of the animal, to the majority that respond most strongly to values that would be produced by sound sources on the contralateral side of space.

Although this continuum of ILD sensitivity matches the distribution of spatial receptive fields in auditory cortex, binaural interactions alone are insufficient to account for the representation of auditory space in the cortex. At near-threshold sound levels, high-frequency AI neurons in cat (Middlebrooks and Pettigrew 1981; Rajan et al. 1990; Brugge et al. 1994) and ferret (Mrsic-Flogel et al. 2003, 2005) tend to have "axial" receptive fields that are centered on the acoustical axis of the contralateral external ear. This is the region in which the acoustical gain of the external ear is at its maximum, therefore suggesting that, at these low sound levels, the receptive fields of the neurons are shaped by pinna directionality. Moreover, using virtual acoustic space stimuli, it has been shown that a linear combination of the frequency sensitivity to stimulation of each ear and the directional properties of the auditory periphery can account
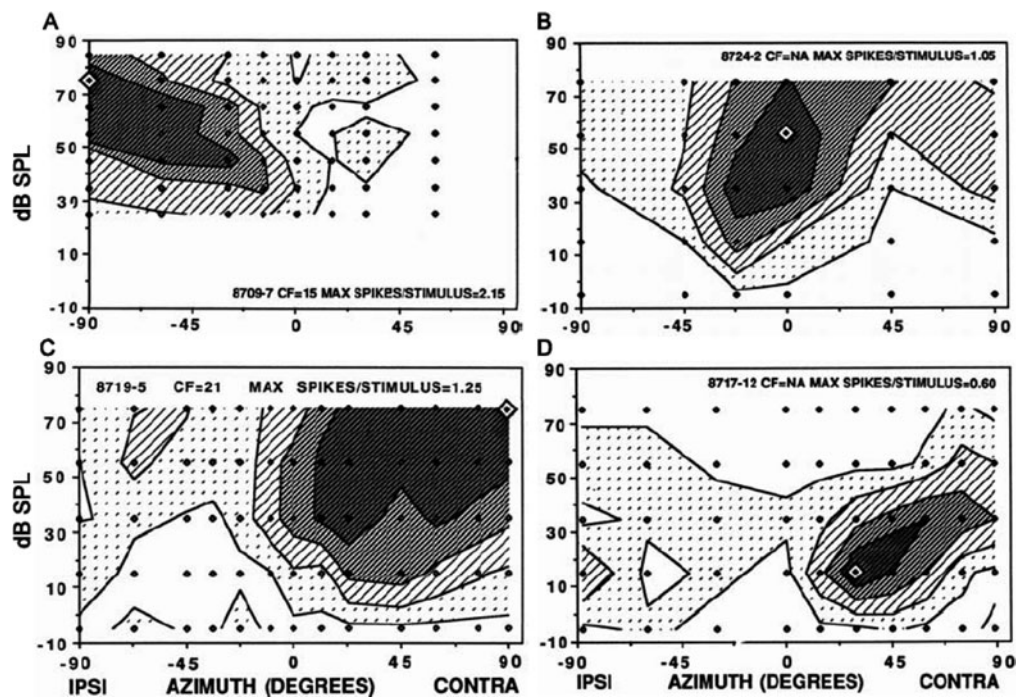
Fig. 15.3 Spatial sensitivity of four neurons in cat area AI. In each panel, contours represent normalized spike rates as a function of sound-source azimuth (*horizontal axes*) and sound level (*vertical axes*). Contours are drawn at 5, 25, 50, and 75% of maximum spike rates. The grids of *small diamonds* indicate stimulus locations and levels that were tested. Adapted from Imig et al.(1990)

for the location and shape of the spatial receptive fields of many high-frequency neurons in ferret AI (Schnupp et al. 2001; Mrsic-Flogel et al. 2005; Fig. 15.4). Changes in spatial sensitivity with increasing sound level can be explained by this linear model (Schnupp et al. 2001; Mrsic-Flogel et al. 2005), which also predicts the observed sharpening of spatial receptive fields with age as the head and ears grow (Mrsic-Flogel et al. 2003). Mrsic-Flogel et al. (2005) found that the linear model works best for neurons that receive predominantly excitatory input from the contralateral ear and inhibitory input from the ipsilateral ear, and which are therefore sensitive to ILDs, but less well for neurons that receive excitatory inputs from both ears and which are likely to be sensitive to ITDs. A similar linear estimation procedure based on the neurons' frequency selectivity and the external ear acoustics can also account for the elevation sensitivity of neurons in the primary fields AI and AAF of the cat cortex (Macpherson et al. 2004).

Several studies have observed that neurons tuned to particular regions of space are found in clusters (Middlebrooks and Pettigrew 1981; Imig et al. 1990; Rajan et al. 1990b), as is also the case for the binaural properties of cortical neurons (e.g., Imig and Adrian 1977; Middlebrooks et al. 1980; Rutkowski et al. 2000; Nakamoto et al. 2004). Although this indicates a degree of local order, there is, in most species, no evidence for a map of auditory space equivalent to that found in the SC or to the spatiotopic maps that characterize the cortices of other sensory modalities. Similarly, optical

imaging of intrinsic signals in ferrets has failed to provide evidence for a systematic variation in sensitivity to ILDs across the cortical surface (Nelken et al. 2008). The only exception to this seems to be in the region of the pallid bat auditory cortex responsible for passive sound localization, where a topographic representation of ILD sensitivity has been described (Razak and Fuzessery 2002).

In addition to changes in firing rate across different loudspeaker locations, variations in the latency of the response can also signal sound-source direction. This has been observed in a number of studies in both anesthetized cats (Middlebrooks et al. 1994, 1998; Brugge et al. 1996; Jenison 2000; Furukawa and Middlebrooks 2002; Reale et al. 2003; Stecker and Middlebrooks 2003) and ferrets (Mrsic-Flogel et al. 2005; Nelken et al. 2005). Although first-spike latencies tend to vary inversely with spike counts, with sounds at preferred locations evoking more spikes with shorter latencies, spike timing can be modulated across the receptive field even at levels at which neurons respond relatively uniformly to all tested locations. Indeed, spike timing can carry as much or more information about sound-source location than spike rate (Brugge et al. 1996; Eggermont 1998; Furukawa and Middlebrooks, 2002; Stecker and Middlebrooks 2003; Nelken et al. 2005).

The proportion of location-related information carried by spike timing is somewhat lower in recordings in unanesthetized conditions (Mickey and Middlebrooks 2003; Woods et al. 2006; Werner-Reiss and Groh 2008). This is likely
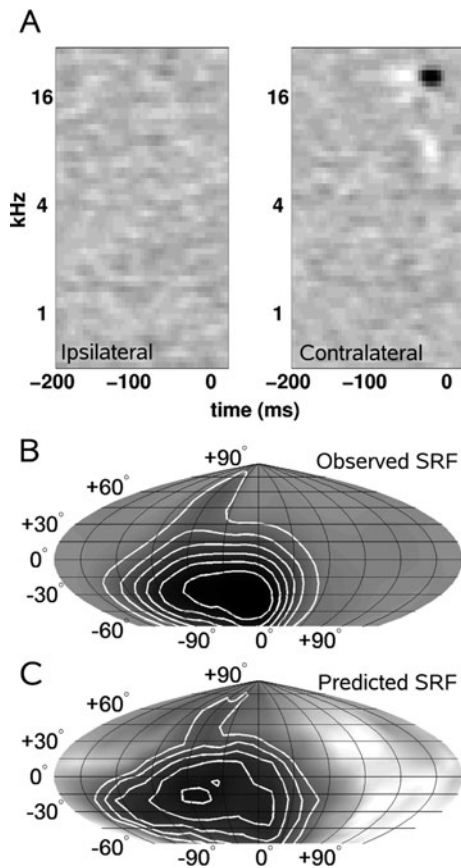
Fig. 15.4 Predicting spatial responses from the frequency tuning of neurons in AI. Examples of frequency-time response fields (FTRFs) for each ear (**a**), together with the observed (**b**) and predicted (**c**) spatial receptive fields (SRFs) of a neuron recorded in AI of an anesthetized ferret. The FTRFs were measured by reverse correlation to random chord stimuli presented to each ear. The observed SRFs were generated by presenting noise bursts from 224 virtual sound directions, covering 360° in azimuth and from –60° to +90° in elevation. The predicted SRFs were generated by convolving the FTRFs with the energy spectrum vectors of the VAS stimuli for each ear and each position in space. From Schnupp et al. (2001)

3.2 Variations in Spatial Sensitivity Across Different Cortical Areas

As discussed above, the impact of cortical inactivation on sound localization depends upon which areas are silenced (Malhotra et al. 2004, 2008; Malhotra and Lomber 2007; Lomber and Malhotra 2008). This apparent division of labor is supported by the results of imaging studies in humans, which suggest that the cortical areas engaged during sound localization are distinct from those involved in sound recognition tasks (Alain et al. 2001; Maeder et al. 2001; Barrett and Hall 2006). A more recent study has reported, however, that widespread cortical areas may be activated during auditory spatial processing (Lewald et al. 2008). The distinction among spatial and non-spatial cortical areas also is less clear cut at the level of neuronal responses, as some degree of sensitivity to sound-source location is a property of all areas that have been examined (Stecker and Middlebrooks 2003; Woods et al. 2006; Harrington et al. 2008; Bizley et al. 2009).

Although there is as yet no evidence for qualitative differences in spatial sensitivity among cortical areas, recording studies have shown that certain cortical areas show quantitatively enhanced spatial sensitivity compared to others. In monkeys, for example, neurons in caudal auditory cortical fields are more sharply tuned for sound-source location than those in core or rostral fields (Recanzone et al. 2000; Tian et al. 2001; Woods et al. 2006; Miller and Recanzone 2009) (Fig. 15.5), which is broadly consistent with most of the imaging data in humans. Similar findings have been obtained in cats, the species in which the representation of auditory space in different cortical fields has been explored most extensively. The spike counts and first-spike latencies of neurons in PAF and DZ show greater modulation with changes in stimulus location and transmit more spatial information, particularly in the timing of their spike discharges, than those in AI, AII, or AAF (Stecker et al. 2003, 2005a; Harrington et al. 2008) (Fig. 15.6c, d). Furthermore, the receptive fields of PAF and DZ neurons are more tolerant to changes in stimulus level than those in other cortical fields.

Although these differences are fairly modest, the distinction between PAF and AAF in cats is supported by the effects of cortical cooling, which results in deficits in sound localization and in sound pattern recognition, respectively (Lomber and Malhotra 2008). Neurons in posterior AES also show greater spatial selectivity compared to those in the AI (Las et al. 2008). Again, this fits with the behavioral-inactivation evidence that AES, which is the only auditory cortical area to project heavily to the SC (Meredith and Clemo 1989), plays an important role in spatial hearing (Malhotra et al. 2004; Malhotra and Lomber 2007). By contrast, the consequences of inactivation of AI are greater than might be expected given the relatively poor spatial sensitivity of its neurons.

to be due to the fact that cortical neurons tend to be more active in the awake condition, providing greater potential for modulation of spike counts by sound-source location, including suppression of spontaneous activity away from the excitatory region of the receptive field. Aside from the deeper stimulus-related modulation of spike rates, spatial sensitivity in unanesthetized conditions is largely similar to that recorded under anesthesia. As in anesthetized conditions, cortical receptive fields recorded in awake animals often span a hemifield in width (Mickey and Middlebrooks 2003; Woods et al. 2006; King et al. 2007), and there is no indication of a point-to-point map of auditory space. One notable difference is that spatial sensitivity is less vulnerable to increases in stimulus level in awake conditions than in the anesthetized state (Mickey and Middlebrooks 2003).

Fig. 15.5 Normalized distribution of activity as a function of stimulus level and azimuth recorded in different areas of the monkey auditory cortex. *Line thickness* and *shading* corresponds to the different levels (see *inset* in **f**). The *horizontal dashed line* is the normalized spontaneous activity. Overall the activity increased with increasing stimulus levels and was more sharply tuned for the caudal belt fields. From Woods et al. (2006)
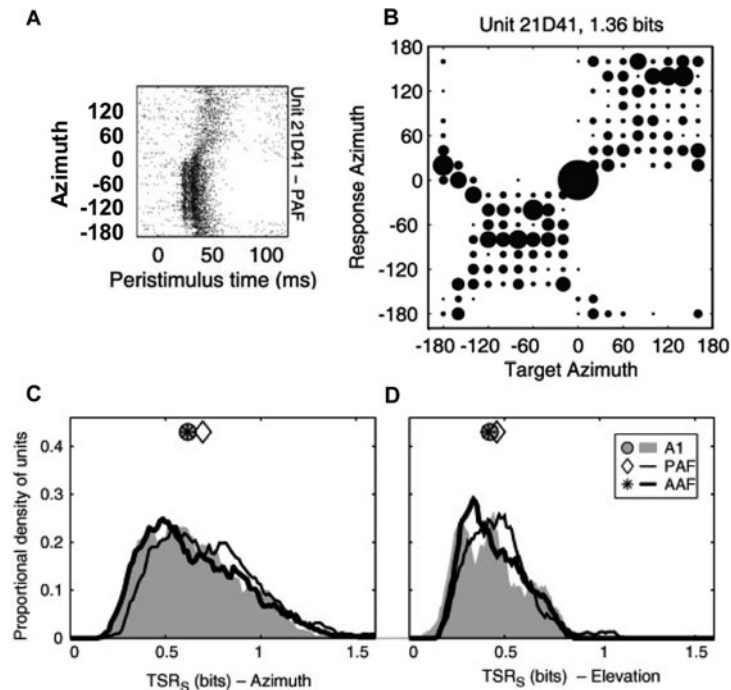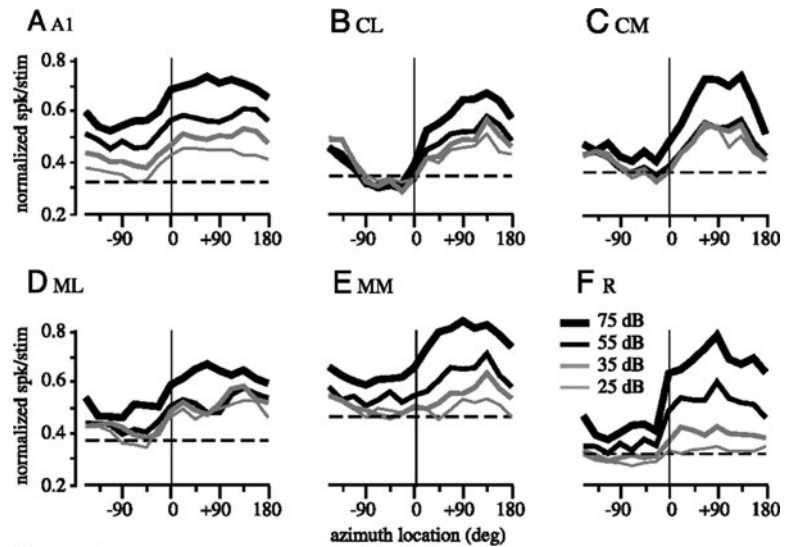

Fig. 15.6 Estimating spatial information carried by neural spike patterns. A statistical pattern recognition algorithm (see Stecker and Middlebrooks, 2003 for details) classifies each neural response according to the most likely eliciting stimulus location. **a** Peristimulus times (*x*-axis) of spikes elicited by stimuli varying in location (*y*-axis) for a neurons recorded in cat area PAF. **b** Algorithm performance for this neuron, represented by a joint stimulus-response matrix (confusion matrix). Proportions of responses at each combination of target (*x*-axis) and response (*y*-axis) location are indicated by the diameter of the *circles* inside the figure. In this case, classification is highly accurate between hemifields: contralateral targets (negative azimuths) are almost never misclassified to ipsilateral locations or vice versa. Targets on the *midline* are accurately localized, although discrimination of front from back is poor. Mutual information of target and response gives an estimate of the total stimulus-related information contained in the neural response; in this case, 1.36 bits. Distributions of total stimulus-related information (TSR) transmitted by neural responses for azimuth (**c**) and elevation (**d**) when full spike patterns were used are shown for neurons recorded in cat AI, AAF, and PAF. *Symbols* represent the median of each distribution. Overall, units in PAF transmit significantly more information than units in AI or AAF. Adapted from Stecker et al. (2003) and Harrington et al. (2008)

The magnitude of these deficits may therefore have less to do with the physiological properties of the neurons in AI than with their projections to other areas, such as PAF (Rouiller et al. 1991). A related possibility is that the responses of AI neurons might provide a temporal reference for comparison with the more pronounced location-related modulations of spike latency in PAF (Stecker and Middlebrooks 2003).

3.3 Encoding Sound-Source Location by Single Neurons and by Neuronal Populations

In order to understand how the activity of cortical neurons might provide a basis for auditory spatial perception, it is necessary to show that a readout of the responses of those neurons can account for the localization ability of the animal. In all species that have been studied, the spatial receptive fields of cortical neurons tend to be broader than behavioral spatial acuity (Brown and May 2005). Moreover, the commonly observed expansion of receptive fields with increasing level contrasts with the finding that sound localization accuracy improves with level close to detection thresholds and then remains relatively constant over a wide range of sound levels (Su and Recanzone 2001; Sabin et al. 2005; Nodal et al. 2008). However, although the region of space within which a stimulus can drive the neurons generally increases, the amount of spatial information conveyed by the responses stays effectively the same (Mrsic-Flogel et al. 2003). A potential advantage of omnidirectional receptive fields is that they provide a means by which the discharge patterns of cortical neurons can convey spatial information across the full range of sound azimuth or elevation, as a result of location-dependent variations in spike count and timing. Indeed, Middlebrooks and colleagues (1994, 1998) have shown that computer-based classifiers can estimate sound-source location from the firing patterns of individual cortical neurons, and that, as expected, the accuracy with which they do so in cats is greatest in areas PAF and DZ (Stecker et al. 2003, 2005a; Harrington et al. 2008) (Fig. 15.6).

Although some cortical neurons have the potential to signal sound-source location throughout auditory space, the accuracy with which they do so falls short of behavioral performance. Similarly, neurometric analyses have demonstrated that the tuning of individual monkey cortical neurons to sound location (Recanzone et al. 2000) or to interaural phase differences (Scott et al. 2009) is not able to account for the acuity measured in behavioral tasks. A consequence of broad tuning is that sounds emanating from a particular direction will activate many neurons distributed throughout the auditory cortex. Several studies have now emphasized the importance of population coding schemes, based either on the full spike discharge patterns (Furukawa et al. 2000; Stecker et al. 2003) or, more specifically, on the spike firing rates (Miller and Recanzone 2009) or latencies (Jenison 2000; Reale et al. 2003) of ensembles of cortical neurons. These population models provide a better fit to the behavioral data. With most receptive fields lying off the midline, the steepest—and therefore most informative—spatial gradients of the neurons' spike counts or latencies lie on or close to the midline (Stecker et al. 2005b; Campbell et al. 2006), which is where localization is most accurate (Makous

and Middlebrooks 1990; May and Huang 1996; Nodal et al. 2008) and spatial discrimination most acute (Mills 1958).

One way in which sound-source location might be represented by the pooled activity of neurons is through an "opponent process," based on the relative activity of two populations of neurons, one tuned ipsilaterally and the other contralaterally (Stecker et al. 2005b). This notion has received support from studies of ITD coding in the brainstem (McAlpine and Grothe 2003) and from psychophysical studies of binaural adaptation in humans (Phillips 2008) where the comparison is thought to be made between activity in the left and right hemispheres. While most cortical neurons do respond preferentially to sounds located on the opposite side of the body, the notion that localization judgments are based on a comparison of activity in the two hemispheres is inconsistent with the contralateral deficits produced in animals by unilateral cortical damage or inactivation (see Section 2). It is possible, however, that an opponent model of sound localization could be based on the contralaterally tuned majority and the relatively few ipsilateral neurons that are found within each hemisphere (Stecker et al. 2005b).

The mode of spatial coding in the auditory cortex raises important questions for how information about sound-source location is combined and coordinated with signals provided by other sensory modalities—which are often represented topographically in the brain—or translated into motor outputs. Neurons sensitive to visual or somatic sensory stimuli have been described in the auditory cortex of numerous species (Ghazanfar and Schroeder 2006). While the function of these non-auditory sensory responses is not fully understood, visual inputs can sharpen the spatial sensitivity of auditory cortical neurons (Bizley and King 2008), and could therefore provide a neural substrate for the many crossmodal influences on spatial perception (King 2009). In monkeys, eye position can also modulate the activity of neurons in the auditory cortex (Werner-Reiss et al. 2003; Fu et al. 2004; Woods et al. 2006). These factors will therefore influence the way in which sound-source location is represented in the auditory cortex.

4 Representation of Multiple Sound Sources

The great majority of behavioral and physiological studies have focused on the localization of single, usually stationary sound sources. While this is the simplest situation to investigate, it is important to remember that real auditory objects are often encountered in reverberant environments and in the presence of other, competing sound sources. Adding diffuse background noise reduces the effective level of the stimuli used to map the responses of cortical neurons and reduces the size of their receptive fields (Brugge et al. 1998;

Furukawa and Middlebrooks 2001). By contrast, background noise originating from a specific direction in space can alter both the size and location of receptive fields (Furukawa and Middlebrooks 2001).

When brief sounds are presented from two different locations, the resulting percept can change if a delay is introduced between them. For delays of less than about 1 ms, human listeners report hearing a single stimulus that originates from a region intermediate between the two source locations, a phenomenon which is therefore known as "summing localization." If the interstimulus delay is extended out to 5 ms, a single sound is still heard, but its perceived location is dominated by the actual location of the leading source. In other words, the percept of the lagging sound is suppressed. This is the "precedence effect," which plays an important role in reducing the influence of room echoes (Litovsky et al. 1999). A neural correlate of these spatial illusions has been observed in the auditory cortex of cats (Reale and Brugge 2000; Mickey and Middlebrooks 2005) and rabbits (Fitzpatrick et al. 1999), although neuronal responses to the lagging sound tend to be suppressed out to much longer interstimulus delays than the precedence effect lasts for in humans.

Ongoing studies are exploring a cortical correlate of "spatial stream segregation," in which sequences of sounds originating from distinct locations are perceived as corresponding to distinct auditory objects. In the cortical work (Middlebrooks et al. 2009), interleaved trains of brief noise bursts are presented from sources at two locations. A spatial separation of as little as 10° can result in the time-locked response of a cortical neuron being captured by one or the other sound source. That spatial acuity is substantially greater than that which has been observed in the responses of cortical neurons mapped with single sound sources.

5 Dynamic Coding of Auditory Space

As with their other response properties, the spatial sensitivity of cortical neurons is not fixed, but depends on the animal's behavioral state and on the neurons' history of stimulation. Dependence on history of stimulation has been demonstrated for sensitivity to interaural phase differences (Malone et al. 2002) and to virtual sound locations (Jenison et al. 2001). These context-dependent effects may enhance the representation of certain stimulus values or confer sensitivity to moving sounds. Ongoing studies of the effects of behavioral state show that the spatial sensitivity of cortical neurons can sharpen markedly under conditions in which an animal is required to localize sounds (Lee et al. 2008).

Over longer time scales, changes in cortical response properties have been shown to accompany improvements in performance during perceptual learning (reviewed by

Dahmen and King 2007). Although plasticity has yet to be demonstrated for spatial sensitivity at the neuronal level, auditory-evoked potential measurements in humans suggest that training-induced improvements in ITD discrimination may be associated with refinements in the cortical population response (Spierer et al. 2007). Auditory cortical plasticity may also enable adult animals to adapt to changes in the balance of inputs between the two ears. Provided that they are given appropriate auditory training, adult ferrets can rapidly adjust to the altered spatial cues produced by occluding one ear and learn to localize accurately again (Kacelnik et al. 2006). The capacity of the animals to compensate for these changes in binaural cues is impaired if different regions of the auditory cortex, including AI, are reversibly inactivated (King et al. 2007) (Fig. 15.7). Sound localization plasticity is also disrupted if a substantial portion of the descending projection from the auditory cortex to the inferior colliculus is removed using a targeted neuronal degeneration technique (King et al. 2007; Bajo et al. 2010) (Fig. 15.7). This finding is consistent with the changes in ILD sensitivity of IC neurons that have been reported in anesthetized guinea pigs following cortical cooling (Nakamoto et al. 2008), and suggests that one function played by the auditory cortex in spatial hearing is to provide signals that are transmitted via descending cortical pathways to bring about experience-driven changes in localization abilities.
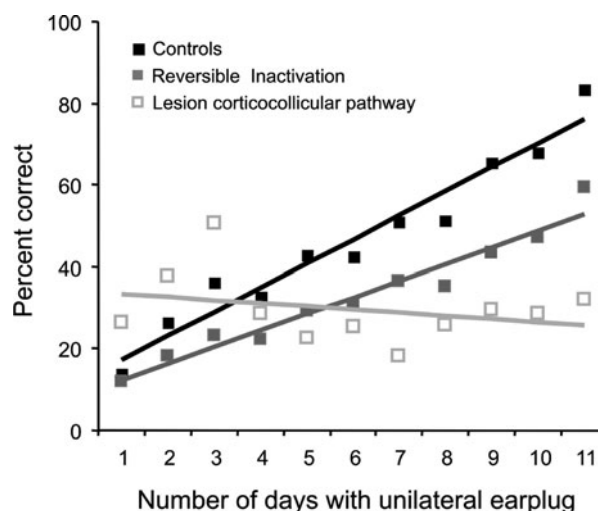

Fig. 15.7 Plasticity of auditory localization depends on the auditory cortex. Change in performance (averaged across all speaker locations, using the setup shown in Fig. 15.1) over time in 3 groups of ferrets that received daily training with unilateral earplugs. Compared to the rapid and near complete recovery in localization accuracy observed in control animals (*n* = 3; *black symbols* and *regression line*), a significantly slower improvement was observed in animals in which AI had been reversibly inactivated using muscimol-Elvax implants (*n* = 4; *dark gray symbols* and *regression line*). Moreover, no improvement in performance was observed in ferrets in which targeted apoptotic degeneration of corticocollicular neurons had been induced using a photoactivation technique (*n* = 3; *open symbols* and *light gray regression line*). Adapted from (King et al. 2007)

6 Concluding Remarks and Future Directions

That the auditory cortex plays an essential role in the ability of many species, including humans, to localize sound is beyond any doubt, but the nature of that role has yet to be fully established. Recording studies have shown that space is represented by neurons possessing very large receptive fields that most often are centered within the contralateral hemifield. The regions of greatest spatial acuity, near the frontal midline, correspond to the edges of many of these large receptive fields. Although sound-source location can be signaled by both the timing and the number of spikes evoked by individual cortical neurons, pooling of this information across populations of neurons appears to be required in order to account for behavioral performance. As with other aspects of auditory perception, further insights into the neural coding strategies used to extract spatial information will only come if recordings are made from cortical neurons, while animals perform localization tasks, so that trial-by-trial correlations can be made between the physiology and the behavior.

While the contribution of different cortical fields to spatial hearing is clearly not the same, with some areas, such as PAF and DZ in cats and the caudal fields in monkeys, showing greater and more level-tolerant spatial sensitivity than others, neurons in all cortical areas convey at least some information about sound-source location. This might simply reflect the processing that takes place subcortically, but it is also possible that the widespread location dependence of cortical processing is just one aspect of a higher-level function, such as the ability to group together sounds that originate from a particular source and to segregate sounds that originate from different sources. Approaching cortical function from this perspective, and focusing on the highly context-dependent nature of the responses found there, should help to answer the enduring question of what the auditory cortex adds to spatial processing performed in the brainstem.

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