

A systematic representation of interaural intensity differences in the auditory cortex of the pallid bat

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The current model of cortical processing of auditory spatial information is based on an orthogonal representation of frequency and binaural response properties, but how this arrangement leads to representation of space in the auditory cortex is unclear. This study describes the first evidence of a cortical substrate for the systematic representation of space in a region of primary auditory cortex of the pallid bat that

subserves passive sound localization. The organizational feature of this region is a systematic shift in sensitivity to interaural intensity differences across the cortical surface, suggesting a topographic representation of horizontal space based on the distribution of activity within the neuron population. *Neuro-Report* 11:2919–2924 © 2000 Lippincott Williams & Wilkins.

Key words: Auditory cortex; Interaural intensity difference; Sound localization

INTRODUCTION

The visual and somatosensory cortices contain inherent representations of space based on a preservation of the topography of their sensory epithelia. In contrast, the fundamental organizational feature of the auditory cortex is cochleotopic, which provides a map of sound frequency. Auditory space must be computed centrally from spatial cues such as interaural time and intensity differences. Unilateral lesions of mammalian auditory cortex reduce sound localization accuracy, indicating that the auditory cortex is indeed important in sound localization [1,2]. However, in contrast to the auditory midbrain, where systematic topographic representations of either spatial sensitivity or binaural localization cues have been reported [3–6], a cortical substrate for a systematic representation of auditory space has not been found. Surveys of spatial sensitivity, using free-field stimulation, report that neurons sensitive to similar sound locations tend to be clustered together, but systematic spatial maps similar to those found in the midbrain were not observed [7–9].

Cortical surveys of neuronal sensitivity to the interaural time and intensity differences, using closed-field dichotic stimulation, also report that neurons are clustered according to binaural type, e.g. clusters of binaurally inhibited neurons occur adjacent to clusters of binaurally excited neurons [10–15]. In the cat and ferret, an orthogonal arrangement of isofrequency contours and binaural clusters occurs, so that each frequency band contains a full complement of binaural types. This clustered organization appears to be a consistent feature of the auditory cortex, but it

remains unclear whether or how this leads to a representation of space. The failure to find an orderly representation of space has led to suggestions that auditory cortex may not represent space through a topographic map. Instead, the auditory cortex may use other neural codes, such as the temporal pattern of firing that may not require a systematic anatomical representation [16].

While it is likely that the auditory cortex uses more than one encoding mechanism for spatial representation, the present study presents the novel finding of a topographic organization of cortical neurons that vary systematically in their sensitivity to interaural intensity differences (IIDs). Consequently, these neurons should also vary systematically in their sensitivity to the horizontal sound locations where these IIDs are created. This IID map is located in a large field of binaurally inhibited neurons tuned to a narrow frequency range. The field appears to be a hypertrophied analog of the binaural clusters observed in other species.

This cluster occurs in the auditory cortex of the pallid bat (*Antrozous pallidus*), a rather atypical bat that uses passive sound localization to locate and capture terrestrial prey, and reserves its echolocation for general orientation [17,18]. It selectively attends to short, prey-generated, noise transients with bandwidths of 1–20 kHz to capture prey. The spectrum of the echolocation pulse is higher and consists of a 60→30 kHz downward frequency sweep. The pallid bat's ability to passively localize sound sources is remarkably accurate [18], with an angular resolution perhaps as great as 1°. The IID map described here is located

within a large field of binaurally inhibited neurons tuned between 8 and 20 kHz, many of which respond selectively to noise transients. The frequency tuning and response selectivity of these neurons strongly suggest that this field subserves the pallid bat's acute passive sound localization behavior.

MATERIALS AND METHODS

Nineteen auditory cortices in 12 bats were extensively mapped to determine the functional organization of a region of the auditory cortex (Fig. 1a) that is located within the primary auditory cortex, based on its tonotopy and connections with the ventral division of the medial geniculate body (W. Shen 1995, M.S. Thesis, University of Wyoming). Due to the need to finely map large regions of cortex, the activity of both single and multiunit clusters were used to determine its functional organization. Little difference was observed in the response properties of single neurons and multiunit clusters obtained in the same electrode penetration.

Surgery and electrophysiological recordings were undertaken in bats anesthetized with metofane inhalation, followed by sodium pentobarbital (30 $\mu\text{g/g}$, i.p.) and acepromazine (2 $\mu\text{g/g}$, i.p.). Surgical techniques and sound generation/neural recording techniques are discussed elsewhere [19]. Using skull and vascular landmarks, neural activity was recorded from single neurons or small clusters of neurons using glass electrodes (1M NaCl; 2–12 M Ω impedance). At each site, best-frequency (BF), response selectivity, IID sensitivity and inhibitory threshold were determined.

The distribution of recording sites were as uniform as possible. At each site, two recordings were obtained at depths between 200 and 600 μm (radial penetration). The response properties did not change significantly with depth at the great majority of recording sites.

Sound stimuli were presented with closed-field, dichotic stimulation via Infinity emit-K ribbon tweeters fitted with funnels that were inserted into the pinnae, and sealed with petroleum jelly to prevent acoustic crosstalk. Best frequencies were determined with 5–10 ms tone bursts. Response selectivity was determined relative to four sounds: pure tones, upward and downward frequency sweeps that encompassed the best frequency, and broadband noise. Criteria for response selectivity were both response thresholds and response magnitudes. If the response threshold for a given stimulus was ≤ 10 dB and/or the response magnitude was $\geq 30\%$ more, then the site is considered selective for that stimulus. FM neurons responded better to a downward 60–30 kHz frequency sweep mimicking the echolocation pulse than to an upward sweep with the same spectrum, a broadband noise containing the same spectrum, or a tone within the spectrum. Noise-selective (N) neurons responded better to a broadband noise burst than to single tones or frequency sweeps through their best frequency.

IID sensitivity was determined by holding the intensity at the contralateral ear constant, and varying the intensity at the ipsilateral ear. The three most common binaural types observed (Fig. 1b) were binaurally inhibited (EO/I) neurons, neurons with mixed binaural inhibitory and facilitatory interactions (EO/FI), and monaural neurons

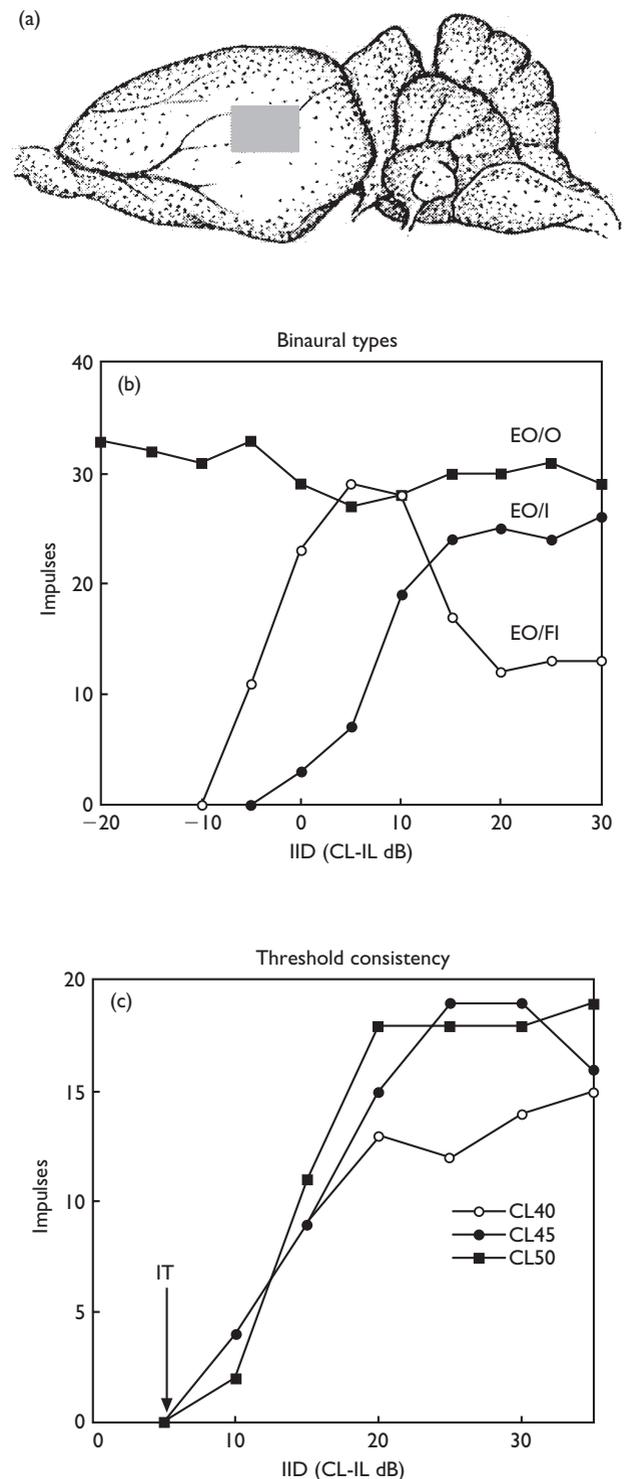


Fig. 1. (a) The brain and auditory cortex of the pallid bat. The figure shows the location of the auditory cortex from which recordings were obtained. (b) The binaural response properties of cortical neurons. The typical IID functions of the three dominant aural types of neurons found in auditory cortex. (c) Three IID functions of an EO/I neuron when the contralateral intensity was fixed at three intensity levels. IT indicates the inhibitory threshold of the neuron, which in this case was the same at all intensity levels. CL indicates the fixed intensity level at the contralateral ear.

(EO/O). All three types were excited by sound at the contralateral ear. Binaural inhibition and facilitation were defined as a >30% decrease or increase in response, respectively, relative to contralateral sound alone. Increasing sound intensity at the ipsilateral ear could either inhibit the neuron (EO/I), inhibit or facilitate the response depending on the IID (EO/FI), or have no effect (EO/O). EO/I neurons had stepped IID functions, with the response typically dropping to zero as the ipsilateral intensity increased. EO/FI neurons had step-peaked IID functions, with the response typically increasing at IIDs near 0 dB and then decreasing as the ipsilateral intensity increased. Binaurally facilitated neurons (EO/F) were relatively uncommon, and showed an increase in response with increasing ipsilateral intensity. Binaurally excited neurons (EE), excited by sounds at either ear, while abundant in the cortices of other species, are rare in the pallid bat auditory cortex.

IID sensitivity was quantified as the inhibitory threshold (IT), defined as the most positive IID at which the neurons are first maximally inhibited (Fig. 1c). A positive IT indicates that a neuron is inhibited when IIDs favor the excitatory contralateral ear, or, put another way, the neuron is completely inhibited even when the relative intensity at the inhibitory ear is weaker. Negative ITs indicate that the intensity must be louder in the inhibitory, ipsilateral ear for maximum inhibition. The EO/I neuron in Fig. 1c provides an example in which the IT consistently occurred at +5 dB IID when IID sensitivity was tested at three fixed contralateral intensity levels.

RESULTS

Tonotopy and response selectivity: Frequency representation proceeds from low to high in a caudolateral to rostromedial direction, from 5 to 70 kHz. Figure 2 shows a representative example of a cortex mapped with respect to the four response properties tested on all cortices: frequency tuning, response selectivity, binaural response properties, and ITs. As was the case in all 19 cortices, the frequency map is not particularly orderly, nor are all frequencies represented equally. A consistent feature in all 19 cortices examined is an under-representation of frequencies between 25 and 35 kHz. The result is a sharp jump in frequency representation. This rapid transition in frequency representation suggests that the tonotopic map in this species is modified to enlarge the representations of those frequencies used in two different behaviors, passive sound localization of prey (1–20 kHz) and echolocation (30–60 kHz).

The different response selectivities of neurons in these two bands of frequency representation support this interpretation. The example shown (Fig. 2b) is an extreme case in that all neurons except one tuned to <32 kHz responded selectively to noise transients that mimicked prey-generated sounds. In contrast, most neurons tuned to higher frequencies preferred downward frequency sweeps of 60→30 kHz that mimicked the echolocation pulse. Within the entire sample of 459 recording sites (408 multiunit clusters and 51 single neurons) in 19 cortices, 79% showed a selectivity for one of these two sounds.

Response selectivity and binaural properties: A striking and consistent feature of the pallid bat auditory cortex is

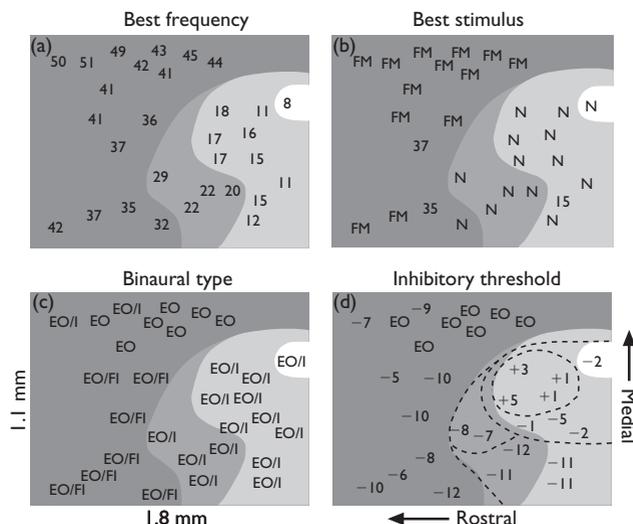


Fig. 2. Functional organization of a representative auditory cortex. (a–d) represent an exposure over part of the auditory cortex that contains both the high-frequency (>35 kHz) echolocation region (anterior) and the low-frequency (<30 kHz) region serving passive sound localization. (a) The frequency map (in kHz) showing the distribution of best frequencies. Shades of gray, from light to dark, show regions tuned to <10 kHz, 10–19 kHz, 20–29 kHz and >30 kHz. The same gray scale is used to indicate frequency representations in Fig. 3. (b) The response selectivity of the same neurons superimposed on the frequency map. N indicates noise-selective neurons. FM indicates neurons selective for the downward frequency sweep of the echolocation pulse. Numerical values indicate the best frequencies of sites that responded best to tones. (c) The binaural response properties of the same neurons, superimposed on the same frequency map. (d) The inhibitory thresholds (ITs) of the same neurons, superimposed on the frequency map. The dashed lines indicate the contours for IT values for noise-selective neurons within the low-frequency region.

the different distribution of binaural response properties exhibited by low-frequency, noise-selective neurons, and high-frequency neurons selective for the downward frequency sweep of the echolocation pulse. The various binaural types are organized in clusters. As seen in Fig. 2c and Fig. 3a,c, a large, homogeneous cluster of EO/I neurons dominates the low-frequency, noise-selective field. A separate, smaller cluster of EO/FI neurons typically occurs in the rostromedial portion of the field (Fig. 3a,c). In contrast, the high-frequency echolocation region contained a large portion of monaural neurons (EO/O) that were typically clustered near the transition zone between low and high frequency representation (Fig. 2c). The distribution of binaural types as a function of frequency tuning is summarized in Fig. 4, which shows that the lower the frequency tuning in the noise-selective region, the greater the percentage of EO/I neurons, while neurons tuned to the echolocation pulse (>30 kHz) represented a disproportionately large percentage of monaural neurons.

Topographical arrangement of IID sensitivity: We focus now on how spatial location may be represented within the large low-frequency, noise-selective region that presumably serves passive sound localization. Our working hypothesis was that EO/I and EO/FI neurons are all maximally inhibited as the relative intensity of the sound

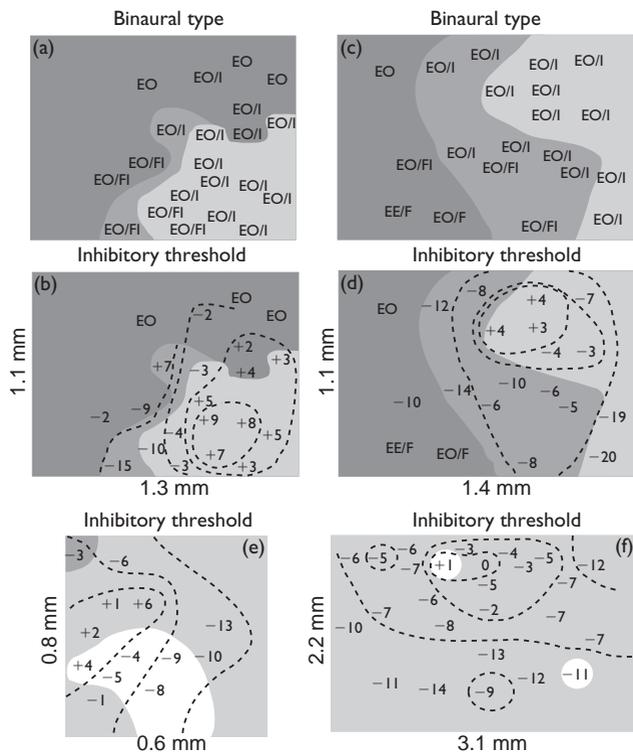


Fig. 3. Four additional examples of the distribution of binaural types and inhibitory thresholds of neurons in the low-frequency, noise-selective region of auditory cortex. The gray shades represent the same best frequency ranges as in Fig. 2. (a and b) and (c and d), respectively, show the binaural types and inhibitory thresholds of two auditory cortices. In both cases, the low-frequency regions are dominated by EO/I neurons, with a smaller cluster of EO/FI neurons located lateral and rostral. (e and f) show only the inhibitory threshold maps of two additional cortices. In both of these latter two cases, the best frequencies are almost entirely < 20 kHz.

at the inhibitory ipsilateral ear increases, that they will be maximally inhibited at different IIDs, and that they may be anatomically organized with respect to their IID sensitivity.

As shown in five examples (Fig. 2d, Fig. 3b–f), EO/I and EO/FI neurons in the low-frequency, noise-selective region are organized with respect to their ITs in a roughly concentric fashion, with a small field of neurons with the most positive ITs surrounded by neurons whose ITs become progressively more negative as they move away from the center. This small region of positive ITs was consistently observed in all cortices studies. As ITs became more negative, the organization of ITs typically became more variable. This concentric organization did not always form a complete circle because, as shown in Fig. 2d, neurons with the most positive ITs were sometimes located immediately adjacent to the high frequency region. Figure 3a,b, and Fig. 3c,d show the clustering of binaural response properties and the distribution of ITs in two other cortices. Figure 3e,f shows two additional examples of only the distribution of ITs.

A neuron’s inhibitory threshold (IT) can be used to estimate its spatial sensitivity. Previous studies [20,21] that used both free-field and closed-field stimulation to relate

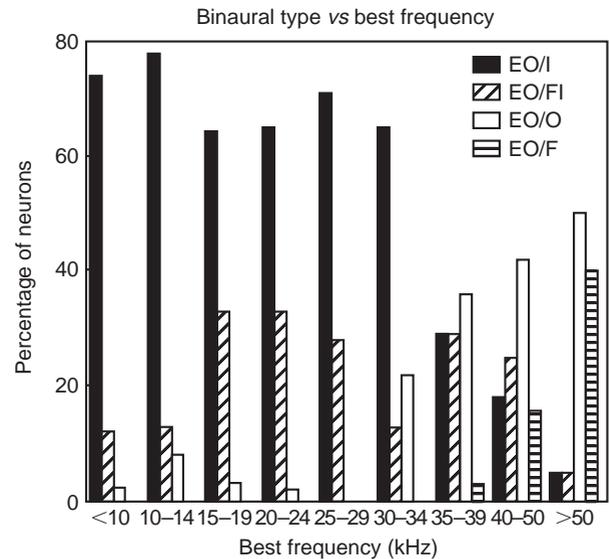


Fig. 4. The relationship between best frequency and binaural type of 429 neurons. EO/I and EO/FI neurons dominated the low-frequency region, while monaural EO/O neurons were common only in the high-frequency region.

binaural response properties to spatial tuning demonstrated that the IT of EO/I and EO/FI neurons determines the location of the medial spatial receptive field borders in the frontal sound field. The distribution of IIDs in the pallid bat’s frontal sound field has been measured (Fig. 5b,c; adapted from [22]), so the receptive field borders of neurons can be estimated with confidence based on their ITs. As ITs become more positive, spatial receptive fields will contract towards the contralateral half of the sound field (Fig. 5). As ITs become more negative, the fields will expand into the ipsilateral half of the field (Fig. 5b).

This systematic organization of IID sensitivity suggests that the borders of spatial receptive fields will also vary systematically across the cortical surface. However, for this to occur, the IID sensitivity of neurons must be stable over a range of absolute intensity levels (e.g. Fig. 1c). If ITs vary significantly with intensity level, then receptive field borders will also vary. To test the stability of IID sensitivity, ITs were measured with the contralateral intensity fixed at least three intensity levels 10–30 dB above response threshold. One measure used to quantify variability is the change in IT relative to the change in absolute intensity level [23]. For example, if the values of the IT of a neuron were 10 dB, 12 dB and 14 dB at contralateral intensities of 35 dB, 45 dB and 55 dB, respectively, then the ratio of IT/intensity range is 0.2 (i.e. (14–10)/(55–35) = 4/20 = 0.2). More than 50% of the low-frequency, noise-selective neurons recorded had a ratio < 0.2, and > 80% of the neurons had a ratio < 0.4. This suggests that these IT maps will remain quite stable over a range of absolute intensity levels.

DISCUSSION

As in other bat species studied (reviewed in [24]), the frequency map in the pallid bat’s primary auditory cortex reflects a task-oriented organization, rather than the more

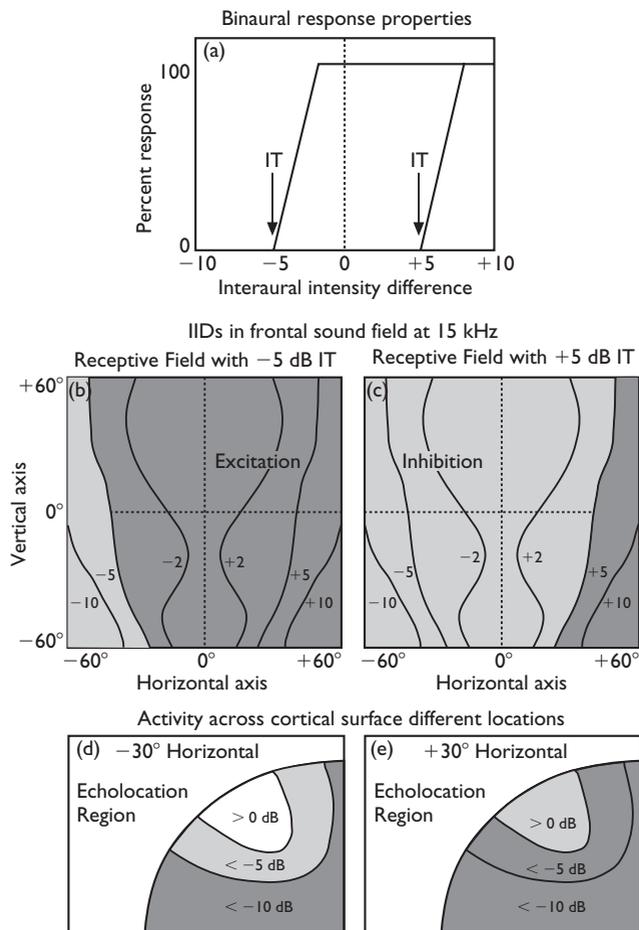


Fig. 5. Schematic figures showing how the systematic distribution of inhibitory thresholds in the noise-selective region might represent horizontal auditory space. (a) The IID functions of two neurons with inhibitory thresholds at -5 dB and $+5$ dB IID. (b,c) The spatial receptive fields of these neurons (red) and the iso-IID contours (solid lines) in the frontal sound field, simplified from data from [22]. Since the neuron with an inhibitory threshold is completely inhibited at IIDs more negative than $+5$ dB, its receptive field will be restricted to the extreme contralateral half of the frontal sound field, where positive IIDs are generated. The neuron with an inhibitory threshold of -5 dB IID will have a much larger receptive field because it is completely inhibited only when a sound is > 5 dB louder in the ipsilateral inhibitory ear (negative IIDs). The IID contours are those produced at 15 kHz, which is roughly at the center of the best frequency range of noise-selective neurons. (d,e) The distribution of active neurons across the cortical surface in the low-frequency, noise-selective region, based roughly on the inhibitory threshold map shown in Fig. 1. The level of activity is indicated by the shade of red, with deep red indicating high activity levels. Horizontal locations refer to those in (b) and (c). (d) When a sound is in the ipsilateral half of the sound field (-30° horizontal), generating negative IIDs, neurons with the most positive inhibitory thresholds (> 0 dB) will be completely inhibited. (e) When the sound is in the contralateral field (30° horizontal), a greater percentage of the neurons will be active, with some neurons with the most positive inhibitory thresholds still not reaching maximum responses, hence the lighter shading.

uniform cochleotopy typical of non-echolocating mammals. Due to its reliance on both echolocation and passive listening, the pallid bat is unusual among the bat species thus far studied in that its frequency map has a hypertrophied representation of low-frequency neurons sensitive to

noise transients used in prey localization, as well as an over-representation of its echolocation spectrum. Within this noise-sensitive region, two binaural types, EO/I and EO/FL, dominate, and they each occur in homogeneous clusters, an organization similar to those observed in other mammalian auditory cortices [11–15]. One intrinsic organizational feature within this region is a topographical arrangement of IID sensitivity, suggesting a systematic representation of auditory space, similar to that reported in the auditory midbrain.

A mechanism that can translate this representation of IID sensitivity into a representation of horizontal auditory space is the same as has previously been suggested for a cluster of EO/I neurons in the hypertrophied 60 kHz region in the inferior colliculus of the mustached bat [5,25]. In this species, the ITs of these neurons change systematically along the vertical axis of the inferior colliculus. Consequently, neuronal activity within this neuronal population will shift along this axis as a sound moves along the horizontal axis of space. When the sound is deep in the excitatory, contralateral half of the sound field, the entire population will be active. As the sound moves towards the ipsilateral half, more neurons will be inhibited, beginning with those with the most positive ITs. Thus the percentage of neurons within the population that are active can encode horizontal sound location.

This population code can also be applied to the auditory cortex, the only difference being that the distribution of active neurons will change systematically across the cortical surface (Fig. 5d,e). A sound deep in the excitatory contralateral field will excite most of the population (Fig. 5e). As the sound source moves ipsilaterally, neurons in the center of the concentric IT map with the most positive ITs will be inhibited first, and the inhibition will spread out radially (Fig. 5d). The opposite hemisphere of the auditory cortex will enhance spatial information, since changes in cortical activity will occur in the opposite fashion. This mechanism can provide both a population code for horizontal space in terms of the percentage of active neurons within the population, and perhaps a place code, since specific regions of the hemispheres will be active or inactive as a function of sound location.

CONCLUSION

The low-frequency, noise-sensitive region of the auditory cortex of the pallid bat possesses a systematic topographic distribution of IID sensitivity. Since IID sensitivity influences the locations of medial receptive field borders, this organization may also represent a systematic change in spatial tuning. Future studies using both closed- and free-field stimulation will verify this assumption. We have therefore suggested that this organization may provide a substrate for a population code for systematic representation of space in the cortex. The proposed model is probably only one component of spatial representation in the pallid bat auditory cortex. Other codes, such as timing of firing across the population, and other spatial information, such as spectral cues, will most likely contribute to a complete spatial representation. It remains to be determined how these additional features may be integrated into the IID map. How this model of spatial representation generalizes to the auditory cortices of other species is unclear, but

given that a clustering of neurons according to binaural type is a common feature of the mammalian auditory cortex, similar representations of space may be found within the intrinsic organizations of these clusters.

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