Modular Functional Organization of Cat Anterior Auditory Field

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1Coleman Memorial Laboratory, W.M. Keck Center for Integrative Neuroscience, Department of Otolaryngology, University of California, San Francisco, California 94143-0732; 2Department of Neurobiology and Physiology, Northwestern University, Evanston, Illinois 60208; and 3Departments of Neuroscience and Otologyngology, University of Florida Brain Institute, Gainesville, Florida 32610-0244

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Imaizumi, Kazuo, Nicholas J. Priebe, Poppy A. C. Crum, Purvis H. Bedenbaugh, Steven W. Cheung, and Christoph E. Schreiner. Modular functional organization of cat anterior auditory field. J Neurophysiol 92: 444–457, 2004. Two tonotopic areas, the primary auditory cortex (AI) and the anterior auditory field (AAF), are the primary cortical fields in the cat auditory system. They receive largely independent, concurrent thalamocortical projections from the different thalamic divisions despite their hierarchical equivalency. The parallel streams of thalamic inputs to AAF and AI suggest that AAF neurons may differ from AI neurons in physiological properties. Although a modular functional organization in cat AI has been well documented, little is known about the internal organization of AAF beyond tonotopy. We studied how basic receptive field parameters (RFPs) are spatially organized in AAF with single- and multiunit recording techniques. A distorted tonotopy with an underrepresentation in midfrequencies (1 and 5 kHz) and an overrepresentation in the high-frequency range was found. Spectral bandwidth (Q-values) and response thresholds were significantly correlated with characteristic frequency (CF). To understand whether AAF has a modular organization of RFPs, CF dependencies were eliminated by a nonparametric, local regression model, and the residuals (difference between the model and observed values) were evaluated. In a given isofrequency domain, clusters of low or high residual RFP values were interleaved for threshold, spectral bandwidth, and latency, suggesting a modular organization. However, RFP modules in AAF were not expressed as robustly as in AI. A comparison of RFPs between AAF and AI shows that AAF neurons were more broadly tuned and had shorter latencies than AI neurons. These physiological field differences are consistent with anatomical evidence of largely independent, concurrent thalamocortical projections in AI and AAF, which strongly suggest field-specific processing.

INTRODUCTION

The cat auditory cortex, like all mammalian auditory cortices, consists of multiple tonotopic areas (Reale and Imig 1980). Physiological evidence indicates that primary auditory cortex (AI) and anterior auditory field (AAF) are the first cortical areas to process auditory information. Neurons in both areas have strong responses to tonal stimuli with short latencies (Knight 1977; Merzenich et al. 1974; Phillips and Irvine 1982). In addition, anatomical studies indicate that these areas are situated at a similar level in the cortical hierarchy (Rouiller et al. 1991). This hierarchical equivalency provides a unique opportunity to study how topographical projections create global and local maps and to compare their physiological properties.

Thalamocortical projections to AI and AAF emanate from separate divisions of the medial geniculate body (MGB) (Andersen et al. 1980; Lee et al. 2004; Morel and Imig 1987; Rouiller et al. 1989). AI receives a majority of its thalamic projections (~80%) from the tonotopically organized ventral division of the MGB (Imig and Morel 1985a; Lee et al. 2004). On the other hand, AAF receives equal proportions (~40 and 35%, respectively) of projections from the tonotopic ventral division and the rostral pole (also termed the lateral part of the posterior group) of the MGB (Imig and Morel 1985b). In addition, AAF also receives a significant proportion (~12%) of thalamic inputs from the nontonotopic dorsal and medial divisions of the MGB (Lee et al. 2004; Rouiller et al. 1989). Furthermore, a double-labeling study after injections of two different retrograde tracers into matched isofrequency domains of AI and AAF shows that <2% of the same thalamocortical projection neurons terminate in both areas (Lee et al. 2004). Therefore the vast majority of thalamocortical projections to AI and AAF originate from different subcortical sources (Lee et al. 2004; Morel and Imig 1987). These current projections may result in differences in physiological properties between AAF and AI. Receptive field properties and their topographic organization have been studied extensively in AI. In AI, neurons are tonotopically organized (Merzenich et al. 1974), and respond either to a restricted or a wide frequency range with relatively narrow dynamic range (Nelken 2002; Read et al. 2001; Schreiner and Mendelson 1990). Neuron clusters with similar physiological properties are nonrandomly distributed along isofrequency contours (Nelken 2002; Read et al. 2002). By contrast, knowledge about AAF response properties is more limited (Eggermont 1998a; Eggermont 1999; Knight 1977; Phillips and Irvine 1982; Schreiner and Urbas 1986) and, in particular, the functional organization beyond tonotopy is little understood.

We studied AAF neural responses and their spatial arrangement by making single- and multiunit recordings from the main thalamocortical recipient layers (layers IIIb and IV) (Huang and Winer 2000) to address the following questions. 1) Do the different thalamocortical projections to AAF distinguish them from AI in spectral representation? Previous evidence has indicated that AI and AAF are mirror images of one another because of their similar tonotopic representations (Knight 1977; Phillips and Irvine 1982). However, the distinct thalamo-
cortical projections may create characteristic differences in their spectral representations. 2) Does AAF have a modular organization? That is, are there interleaved clusters of neurons with similar physiological properties (Read et al. 2002)? In cat, owl monkey, and squirrel monkey, AI, it is known that there are modular organizations of several receptive field parameters (RFPs), including spectral bandwidth, minimum threshold, and binaural sensitivity (Cheung et al. 2001; Imig and Adrián 1977; Middlebrooks et al. 1980; Read et al. 2001; Recanzone et al. 1999; Schreiner 1998; Schreiner et al. 2000). However, it is not known whether such a modular organization exists in AAF. 3) Do RFPs in AAF and AI differ? Several studies have shown that the physiological properties of AAF neurons are remarkably similar to, or have only small differences from, those of AI neurons (Eggermont 1998a; Knight 1977; Noreña and Eggermont 2002; Phillips and Irvine 1982; Valentine and Eggermont 2001). Other studies provide evidence for some differences in physiological properties between AAF and AI (Kowalski et al. 1995; Linden et al. 2003; Rutkowski et al. 2003; Schreiner et al. 1988). To explore functional differences between AAF and AI, it is appropriate to compare the AAF and AI in the same hemisphere and under similar conditions. The current systematic mapping study of AAF provides a basis for elucidating functional differences between early auditory cortical areas.

METHODS

Surgery and animal preparation

Experiments were conducted on 7 hemispheres (3 left and 4 right hemispheres) from 5 adult female cats. All protocols were approved by the University of California at San Francisco Committee on Animal Research in accordance with federal guidelines for care and use of animals in research. Animals were sedated by intramuscular injections of a mixture of ketamine (22 mg/kg) and acepromazine (0.11 mg/kg). After venous cannulation, sodium pentobarbital (15 mg/kg) was administrated to prevent wound infection, dexamethasone (1.2 mg/kg) and atropine (0.05 mg/kg) was administered and supplemented as needed throughout the surgical procedure. After tracheotomy, a craniotomy was performed to expose the ecosylvian gyrus. The dura mater was partially removed, and the cortical surface was covered with viscous silicone oil. Before commencing the electrophysiological recordings, sodium pentobarbital anesthesia was replaced with a continuous intravenous infusion of a mixture of ketamine (2–10 mg/kg/h) and diazepam (0.05–0.2 mg/kg/h) in lactated Ringers (1–3 ml/kg/h). To prevent edema and mucus secretion, dexamethasone (1.2 mg/kg) and atropine sulfate (0.04 mg/kg) were subcutaneously injected twice a day. Because recordings lasted for 3 to 4 days, an antibiotic, cephalosporin (11 mg/kg, intravenous), was administrated to prevent wound infection. Body temperature was monitored and maintained by a water heating pad at 37 ± 1°C. Electrocardiogram and respiration were monitored continuously during the surgery and recording procedures.

Acoustic stimulus

Experiments were conducted in a double-walled, anechoic chamber (Industrial Acoustics, Bronx, NY). Stimuli were delivered by a STAX-54 headphone through a sealed tube into the acoustic meatus contralateral to the studied hemisphere. The system frequency transfer function was flat (±6 dB), ±14 kHz, and rolled off 10 dB/octave at higher frequencies. Sound stimuli of 50-ms duration (including 3-ms linear rise and fall time) were generated at an interval of 400–750 ms by a microprocessor (TMS32010, 16-bit resolution and 120 kHz D/A sampling rate). Pure tone or white noise bursts were used as search stimuli.

Frequency response areas were mapped by presenting 675 pseudo-randomized tones bursts at different frequencies (45 different frequencies in 3- to 5-octave range) and sound levels (70 dB range in 5-dB steps).

Recordings

Parylene- or epoxylike-coated tungsten microelectrodes (Micro Probes, Potomac, MD or Frederic Haer and Co., Bowdoinham, ME) with 0.5- to 4-MΩ impedance at 1 kHz were used for single- and multunit recordings. Single or double microelectrodes were advanced perpendicularly to the cortical surface with a hydraulic microdrive (David Kopf Instruments, Tujunga, CA). A video picture of the cortical surface was captured and digitized with a CCD digital camera (Cohu, San Diego, CA). Each recording site was marked on the digitized picture using Canvas software (Deneva, Miami, FL). The marked sites were used to reconstruct tessellation maps of the recording area (see following text). Neuronal activity was obtained in layers IIIb and IV (700–1,100 μm below the pial surface). Action potentials were amplified and band-pass filtered (0.3–10 kHz; World Precision Instruments, Sarasota, FL, and Axon Instruments, Union City, CA), fed to an oscilloscope, and isolated from background noise with a time/amplitude window discriminator (BAK). Spikes occurring in the first 50 ms after stimulus onset were recorded at 10-μs resolution for offline analyses.

Data analysis

Data were analyzed using the MATLAB (MathWorks, Natick, MA) platform. StatView (SAS Institute, Cary, NC) was used for statistical analysis.

We describe the functional organization of cat AAF according to a number of RFPs. Excitatory frequency response areas were estimated by weighted 9-point smoothing/averaging. Spike counts at the lowest or highest sound pressure level (SPL, re. 20 μPa) or at lowest or highest frequencies tested were smoothed either by 5 or 3 neighboring points.

Threshold was defined as minimum excitatory SPL, and estimated at 5-dB resolution. Characteristic frequency (CF) was defined as the frequency at which a neuron cluster or a single neuron produced sound-evoked spikes at threshold sound level. Quality factors, a measurement of tuning sharpness, were calculated as CF divided by bandwidth at 10 dB (Q10), 20 dB (Q20), 30 dB (Q30), or 40 dB (Q40) above threshold: the higher the Q-value, the more sharply tuned are the neurons. Minimum latency (hereafter latency) was determined as the minimum value in the latency-level function at CF.

Tessellation map. To reconstruct the spatial distribution of RFPs on the cortical surface, tessellation maps were calculated. The polygon surrounding each electrode penetration in the tessellation map characterizes the area assigned to the functional parameter obtained at the recording site. Borders between neighboring polygons were determined by the midpoints of a straight line between adjacent recording points (Kilgard and Merzenich 1998). The value of each RFP in the cortical surface map is illustrated by color code (e.g., Fig. 1).

Residual smoothing. A goal of this study is to understand how different RFPs are distributed in cat AAF. To eliminate general covariations of RFPs with CF, the differences (residual values) between fitted (predicted) and experimental (observed) values were obtained (Cheung et al. 2001). CF dependency of each RFP was fitted with a nonparametric, local regression model of 0.75 vicinity span. Although finer vicinity spans (0.35–0.65) were also examined, changing the local weightings did not alter the global distribution of residuals. Raw values and residual values smoothed by a weighted least-squares linear regression model of each RFP distribution are displayed as tessellation maps.
RESULTS

AAF is, in general, located between the suprasylvian sulcus (sss) and the anterior ectosylvian sulcus. It is characterized by a tonotopic organization with a gradient opposite of the AI tonotopy expressed as a reversal of the frequency gradient at the AI/AAF border (Knight 1977; Reale and Imig 1980). Figure 1 illustrates the position and tonotopic organization for AI and AAF in a CF tessellation map. In this case, AI and AAF shared 9 units at the border, and these units were included in both areas for analysis.

Extracellular recordings were obtained from 571 single- and multunit in AAF of 7 hemispheres. Recordings were restricted to the exposed gyral surface and did not include the banks of the suprasylvian or anterior ectosylvian sulci to minimize potential biases based on response differences from different cortical laminae often encountered in tangential penetrations. At each site, a frequency response area was obtained, and its basic RFPs were extracted. Penetration number for the recordings, size of mapped areas, and ranges of RFPs for all cases are summarized in Table 1.

Spectral representation in AAF

A clear tonotopic organization was seen in all cases (Figs. 1 and 2). Typically, the transition from AI to AAF evidenced by the reversal of the frequency gradient is located approximately 1–2 mm caudal to the anterior ectosylvian sulcus, although individual variations can be substantial (Knight 1977). Comparison of the frequency gradient in AI and AAF (Fig. 1) indicated a much steeper CF gradient in AAF, likely reflecting the smaller size of AAF as it appears on the cortical surface. In addition, it becomes apparent that the AAF frequency gradient is less uniform with underrepresentation of some CF ranges. This phenomenon was originally found in the bank of the anterior ectosylvian sulcus of cat AAF (Reale and Imig 1980).

In the example illustrated in Fig. 1, the frequencies represented by yellow to orange hues (~10–15 kHz) were nearly absent in AAF, whereas they were clearly present in AI. This underrepresentation of some CF range was observed in all cases. Four representative cases with dense mapping are illustrated in Fig. 2A. In case 426R, green or yellow hues representing about 3–6 kHz occupy smaller areas than other hues. For other cases, CF of approximately 2–4 kHz (light blue) is underrepresented in the tessellation maps. To quantify this observation, the underrepresented CF ranges were estimated by using the cumulative polygon areas in the mapped AAF. If the CF range is distributed evenly from low to high frequencies, the cumulative area curve should be smooth and monotonic. By contrast, if there is an underrepresentation of a particular CF range, the local slope should become shallower for that CF range. Each polygon area was computed and normalized to the entire mapped area. As expected from the observations, the slopes in the midfrequency range (2–6 kHz) are shallow for all 4 cases (Fig. 2B). In addition, some cases showed shallower slopes for low- and midfrequency ranges, 0.5–1 kHz and 10–15 kHz, respectively. For comparison, 2 AI cases are illustrated by gray and dark-pink lines in Fig. 2B (an example shown by a dark pink line was obtained from our ongoing study; Imaizumi and Schreiner

![Image](http://jn.physiology.org/)

FIG. 1. Location of anterior auditory field (AAF) and primary auditory cortex (AI) and the reversal of characteristic frequency (CF) gradient. AAF and AI are located below the suprasylvian sulcus. Three different sulci are illustrated by thick black lines. CF gradient was reconstructed on the cortical surface by Voronoi–Dirichlet tessellation, smoothed by a weighted least-squares linear regression model (see METHODS), and coded by a color scale. Approximate AI/AAF border is illustrated by a dashed line. Border was estimated based on the highest CFs in neighboring polygons. sss, suprasylvian sulcus; aes, anterior ectosylvian sulcus; pes, posterior ectosylvian sulcus; D, dorsal; A, anterior. Scale: 1 mm.

TABLE 1. Receptive field parameters and their ranges in each AAF

<table>
<thead>
<tr>
<th>Case</th>
<th>Penetration Number</th>
<th>Mapped Area, mm²</th>
<th>CF, kHz</th>
<th>Threshold, dB SPL</th>
<th>Q10</th>
<th>Q40</th>
<th>Latency, ms</th>
</tr>
</thead>
<tbody>
<tr>
<td>426L</td>
<td>102</td>
<td>7.2</td>
<td>0.3–35.0</td>
<td>2.5–57.5</td>
<td>0.16–15.7</td>
<td>0.14–13.8</td>
<td>7.9–23.8</td>
</tr>
<tr>
<td>426R</td>
<td>81</td>
<td>6.4</td>
<td>0.2–25.4</td>
<td>7.5–67.5</td>
<td>0.49–32.0</td>
<td>0.22–14.7</td>
<td>7.5–35.3</td>
</tr>
<tr>
<td>101R</td>
<td>58</td>
<td>9.0</td>
<td>1.5–49.5</td>
<td>7.5–52.5</td>
<td>0.24–12.2</td>
<td>0.11–1.4</td>
<td>7.3–28.0</td>
</tr>
<tr>
<td>098R</td>
<td>46</td>
<td>9.2</td>
<td>0.7–46.6</td>
<td>2.5–67.5</td>
<td>0.51–7.4</td>
<td>0.11–19.0</td>
<td>8.0–32.8</td>
</tr>
<tr>
<td>111L</td>
<td>134</td>
<td>15.4</td>
<td>0.4–42.5</td>
<td>−2.5–52.5</td>
<td>0.19–7.6</td>
<td>0.07–4.7</td>
<td>6.2–15.4</td>
</tr>
<tr>
<td>073L</td>
<td>76</td>
<td>9.9</td>
<td>0.6–38.8</td>
<td>−7.5–42.5</td>
<td>0.12–16.8</td>
<td>0.11–1.6</td>
<td>7.6–12.6</td>
</tr>
<tr>
<td>073R</td>
<td>74</td>
<td>10.6</td>
<td>0.5–42.8</td>
<td>−2.5–52.5</td>
<td>0.37–21.1</td>
<td>0.24–1.8</td>
<td>8.1–15.7</td>
</tr>
</tbody>
</table>
As expected, the CF representation in AI is smooth and covers the CF range from low to high frequencies (Merzenich et al. 1974). However, the slope is shallower at low frequencies, reflecting general overrepresentation of higher CFs (Merzenich et al. 1974). Nevertheless, unlike AAF, local steps in the low frequencies were not observed.

To quantify the underrepresented CF ranges in AAF, we used a more objective criterion by calculating the cumulative area in a sliding window of 1/3 octave width. If the summed polygon areas within the window were <3% of the total area, the CF range was considered underrepresented (open circles in Fig. 3, A and B). CF ranges falling below this criterion are marked by horizontal lines in Fig. 3, C and D, and were consistent with the CF ranges of shallow slopes (Fig. 2B). The underrepresented CF ranges for all cases are summarized in Fig. 4. Here, we asked two questions: 1) Do the left and right hemispheres from the same animal have similar underrepresented CF ranges? 2) Is the underrepresented CF range consistent across cases? In case 426, about 3–8 kHz and 11–15 kHz were common ranges for underrepresentation in both hemispheres (Fig. 4A). In case 073, the underrepresented CF range between the hemispheres was shared between about 2 and 5 kHz. Across the cases, underrepresented CF ranges appear to be most likely between 1 and 8 kHz (Fig. 4A). The occurrence of the underrepresented CF range was summed in quarter-octave steps from 0.2 to 50 kHz (Fig. 4B). Consistent with our observations, a majority of cases had underrepresented CF ranges between 1.3 and 5 kHz and about 11 kHz.

**Fig. 2.** A: CF gradient in 4 different AAFs. For the presentation, left and right hemispheres are aligned in the same direction. Case number is shown on the top right for each case. See Fig. 1 legend for abbreviations. B: cumulative areas for 4 different AAFs and 2 AI. Case 073 was derived from the left and right hemispheres in the same animal (indicated with the squares). AI cumulative areas are illustrated by the gray and dark pink lines.
Overrepresentation was observed in the high-frequency range between 20 and 30 kHz (Fig. 3, A and B) (Knight 1977). It is still unresolved whether the smaller size of AAF reflects a reduced spectral magnification factor in AAF compared with AI (Knight 1977) or is related to the underrepresentation of certain CF ranges.

Characteristic frequency-dependent receptive field parameters

RFPs often covary with CF (Cheung et al. 2001; Mendelson et al. 1997). Given the differences in CF distribution between AI and AAF, it is necessary to account for the CF dependency.
in the RFP distribution in the comparison of functional field differences. Figures 5 and 6 illustrate the covariation of RFPs with CF for 2 cases. In Fig. 5, 2 local regression estimates with different vicinity weightings were illustrated (0.75 and 0.35 vicinity spans shown by black and gray lines, respectively). Changing the spread of local weightings did not substantially alter global distribution of residuals (note the logarithmic scale for Q10 or Q40 in Fig. 5). In AAF, the most sensitive CF range (lowest thresholds) occurs at 10–20 kHz, and thresholds increase toward lower or higher CFs. Tuning sharpness property can be expressed by Q10 or Q40 values: the higher the Q-values, the more sharply tuned are the neurons. Q-values increase with CFs. Latency is an RFP that reflects internal integration properties (Heil and Neubauer 2003), conduction and processing delays (Salami et al. 2003), as well as sound localization-related information (Eggermont 1998b; Furukawa et al. 2000). In these two examples (Figs. 5 and 6), AAF neurons tuned to low or high frequency had longer latencies, whereas AAF neurons with CF of about 10 kHz had the shortest latencies. Other cases (4 out of 7) showed no clear CF-dependent latencies (ANOVA: *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001; N.S., not significant; N.A., not available).

**Modular organization of receptive field parameters**

Functional and structural organization of a cortical field can be revealed by the spatial RFP gradients or clusters. RFPs uncorrected for CF (Table 2), however, may exhibit systematic gradients of RFPs that just reflect the influence of tonotopicity. Indeed, raw RFP distributions across the cortical surface show spatial gradients and/or clustering of similar parameter ranges (Fig. 7, A–E). Neurons with high threshold were clustered in the low-frequency area (Fig. 7B), and neurons with high Q10 values (sharply tuned neurons) were clustered in the high-frequency area (Fig. 7C). However, patchy distribution of neurons with high Q10 values can also be seen in the low-frequency area (Fig. 7C). Similarly, nonhomogeneous distributions are discernable for Q40 values (Fig. 7D) and latencies (Fig. 7E).

In cat AI, CF-independent spatial clustering of RFP values is found along isofrequency contours (Heil et al. 1992; Mendelson et al. 1997; Read et al. 2001; Schreiner and Mendelson 1990; Schreiner et al. 2000). To assess the CF-independent RFP distributions in AAF, covariations of RFPs with CF were eliminated by nonparametric, local regression fits (0.75 vicinity span) as presented in Figs. 5 and 6. Spatial distributions of residual RFP variables were smoothed by a weighted least-squares linear regression, and are illustrated as tessellation maps (Figs. 7, F–I, 8, B–E and G–J). If there is no RFP

**TABLE 2. CF dependency of receptive field parameters**

<table>
<thead>
<tr>
<th>Case</th>
<th>Threshold</th>
<th>Q10</th>
<th>Q20</th>
<th>Q30</th>
<th>Q40</th>
<th>Latency</th>
</tr>
</thead>
<tbody>
<tr>
<td>426L</td>
<td>N.S.</td>
<td>****</td>
<td>****</td>
<td>****</td>
<td>****</td>
<td>N.S.</td>
</tr>
<tr>
<td>426R</td>
<td>***</td>
<td>**</td>
<td>N.A.</td>
<td>****</td>
<td>****</td>
<td>N.S.</td>
</tr>
<tr>
<td>101R</td>
<td>***</td>
<td>****</td>
<td>****</td>
<td>****</td>
<td>****</td>
<td>N.S.</td>
</tr>
<tr>
<td>098R</td>
<td>***</td>
<td>****</td>
<td>****</td>
<td>N.S.</td>
<td>N.S.</td>
<td>N.S.</td>
</tr>
<tr>
<td>111L</td>
<td>****</td>
<td>****</td>
<td>****</td>
<td>**</td>
<td>***</td>
<td>*</td>
</tr>
<tr>
<td>073L</td>
<td>****</td>
<td>****</td>
<td>****</td>
<td>****</td>
<td>****</td>
<td>***</td>
</tr>
<tr>
<td>073R</td>
<td>****</td>
<td>***</td>
<td>****</td>
<td>****</td>
<td>****</td>
<td>N.S.</td>
</tr>
<tr>
<td>Total</td>
<td>6/7</td>
<td>7/7</td>
<td>6/6</td>
<td>6/7</td>
<td>5/7</td>
<td>3/7</td>
</tr>
</tbody>
</table>

ANOVA: *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001; N.S., not significant; N.A., not available.
variation in a given isofrequency contour, the tessellation map would show a constant color (e.g., green to yellow hues). If there is a random RFP distribution in a given isofrequency contour, there would be color variations without an apparent clustering. By contrast, if there is clustering of RFP values, it is expected to yield systematic color variations in the tessellation map. In smoothed residual RFP tessellation maps (Figs. 7, F–I and 8, B–E and G–J), regional clusters of similar parameter values are visible.

In the residual Q10 and Q40 maps (Figs. 7, G and H and 8, C and D and H and I), clusters occur in different frequency regions and in restricted portions of the isofrequency domains. This indicates that, for certain frequency ranges, the full extent of Q-values is available for spectral analysis. Similar patchy organizations are apparent for residual maps for latency (Figs. 7, F and I and 8, C and D and H and I), or high residual Q10 (or Q40) values appear at locations with high residual latency (Fig. 8, C–E and H–J). To examine whether such covariations are a general phenomenon across all cases, a factor analysis was conducted for the CF-corrected RFPs (threshold, Q10, Q40, and latency) by pooling across 7 cases. Based on eigenvalues > 1.0, 2 independent factors emerged (Table 3). Factor 1 reflects the co-variation of the 2 spectral-bandwidth measures, Q10 and Q40. Factor 2 reflects threshold as its main contribution. The 2 factors indicate that, across animals, spectral integration and response sensitivity are independent variables. Latency showed a weak correlation with both, Q10 (or Q40) and threshold, in a pooled population. In some individual cases, correlations either between latency and Q10 (or Q40) or latency and threshold were significant (data not shown). However, that trend was not prominent in the pooled data. In summary, local clustering in AAF is evident for threshold, spectral bandwidth (Q-values), and latency. Spectral integration RFPs (Q10 and Q40) appear to be independent from response sensitivity (threshold), which is consistent with RFPs in owl monkey (Recanzone et al. 1999) and squirrel monkey AI (Cheung et al. 2001).

A comparison of receptive field parameters between AAF and AI

AAF and AI receive largely independent, concurrent thalamocortical projections from the different thalamic divisions (Andersen et al. 1980; Lee et al. 2004; Morel and Imig 1987; Rouiller et al. 1989). These different thalamic origins may create differences in receptive field properties for these 2 areas. To compare RFPs between AAF and AI, it is appropriate to have data sets from the same hemisphere and obtain them under similar conditions. Figure 9 illustrates the RFP distributions for AI and AAF obtained from the same cortical hemisphere of case 111L. Because RFPs are CF-dependent, the comparison was limited to a CF range (>10 kHz) that was sufficiently mapped in both fields (Fig. 9A). For this case, AI and AAF shared 6 units at the border that were included in both areas for comparison. There was no difference in CF distributions between AAF and AI (Fig. 9A). A significant difference between the two fields was found for response threshold (Mann–Whitney U test: $P = 0.0497$; Fig. 9B) with slightly lower thresholds in AAF. AAF units were also significantly more

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**Fig. 6.** Distributions of RFPs as a function of CF (case 073L). Black line represents a nonparametric, local regression fit using 0.75 vicinity span. Overall trends are similar to case 111L (Fig. 5). Units with CF between 1 and 4 kHz were sparsely represented. See Fig. 5 legend for explanation and Table 2 for the statistical results.
broadly tuned than AI units (Fig. 9, C and D). Over all frequencies, there was no significant difference for latency between AAF and AI (Fig. 9E).

In most mapped hemispheres (e.g., Fig. 1), AI and AAF were not equally sampled because of constraints in time or unfavorable surface features. Accordingly, we pooled field data across different hemispheres and compared RFP values between AI and AAF in CF bins of one octave (1 to 64 kHz), which can eliminate CF dependency. The AAF cases in this study (n = 7; 461 units) were compared with 16 AI cases (1,435 units) from previous and ongoing studies in the laboratory for which the desired RFPs were available (Imaizumi and Schreiner 2004; Lee et al. 2004; Read et al. 2001; Schreiner and Raggio 1996). Figure 10 illustrates box plots for each RFP distribution. The compared CF bins were evenly sampled except for two low CF bins (1–2 and 2–4 kHz) and one high CF bin (16–32 kHz). These CF bins correspond to under- and overrepresented CF ranges in AAF (Figs. 3 and 4). Thresholds were similar.
between AAF and AI except for a low (2–4 kHz) and high CF bins (16–32 and 32–64 kHz) at which AAF neurons had significantly higher threshold than AI neurons. AAF neurons were more broadly tuned to frequency than AI neurons in most CF bins except for the lowest (1–2 kHz) and highest CF bins (32–64 kHz for Q10). In the mid-CF range, many sharply tuned neurons form prominent modules in AI (Read et al. 2001; Schreiner et al. 2000), which may account for the significant difference of tuning sharpness properties. AAF neurons had shorter latency than AI neurons in all CF bins except for the highest frequencies (32–64 kHz). This may explain the nonsignificant difference for latency between AAF and AI in the single hemispheric comparison that was limited to mid- and high frequencies (Fig. 9).

Overall, concurrent thalamocortical topographical projections are reflected in differences in modular organization and

receptive field properties between AAF and AI, although the main ranges of basic RFPs are highly overlapping.

DISCUSSION

Cat auditory cortical areas AAF and AI are both tonotopically organized and have a largely overlapping spectral representation and similar basic physiological properties (Eggermont 1998a; Knight 1977; Phillips and Irvine 1982). However, our results suggest that AAF differs from AI in several properties despite their hierarchical equivalency. Small but systematic differences in modular organization, frequency organization, and distribution of RFP values combined with anatomical evidence (Lee et al. 2004) strongly indicate that AI and AAF are largely independent, concurrent streams of auditory information.

Modular organizations of AAF

We found a modular organization of RFPs within AAF; that is, RFP values other than CF tended to form interleaved spatial clusters similar to findings in cat and new world monkey AI. However, this organization is less prominent than in AI (Read et al. 2001; Schreiner et al. 2000). Because AAF receives convergent thalamocortical projections from 2 tonotopic and 2 nontonotopic thalamic divisions, whereas AI has a major tonotopic thalamic source, the differences in modular organization between AAF and AI may be accounted for by the differences in thalamocortical projections.

A modular organization in cat AI is conspicuous for binaural response classes (Imig and Adrián 1977; Middlebrooks et al. 1980) and, in particular, for spectral bandwidth (e.g., Q40) (Imaizumi and Schreiner 2004; Read et al. 2001; Schreiner and Mendelson 1990; Schreiner et al. 2000). In AAF, a large module of high Q-values is located within isofrequency contours (Imaizumi and Schreiner 2004; Read et al. 2001; Schreiner and Mendelson 1990). In AAF, several smaller clusters of high or low Q-values were often found along some isofrequency contours. Unlike AI, the location and frequency association of these clusters varied widely within AAF, and the size of the clusters appeared smaller. Because AAF neurons can integrate spectral information over wider spectral bands than AI, the Q-modules in the 2 fields may emphasize different sound aspects in analysis and representation.

Circumscribed clusters of neurons with shorter or longer latency are commonly encountered in AAF. In AI isofrequency contours, neurons with longer latencies are usually found in dorsal and/or ventral areas, whereas neurons with shorter latencies are clustered in the central or ventral areas of AI (Imaizumi and Schreiner 2004; Mendelson et al. 1997). The spatially clustered organization for latency is not as consistent as that for spectral bandwidth in AI. Although the modular latency organization in AAF is somewhat similar to AI (Mendelson et al. 1997), the global temporal response pattern may be distributed uniquely or differently in these 2 primary auditory fields. Latency may provide information about relative timing between different processing steps (Eggermont 1998b; Furukawa et al. 2000). The overall shorter latencies of AAF can also furnish a reference for spike timing for other cortical areas (Stecker and Middlebrooks 2003), although such a reference is not used for sound localization (Lomber and Malhotra 2003).

Local clusters of neurons with similar response threshold are also distributed across AAF. The locations of these clusters show no systematic relationship to spectral bandwidth and latency clusters. The functional significance of regions differing in response sensitivity is not entirely clear. Contributions to the spatial coding of stimulus intensity are conceivable as well as roles in signal detection and discrimination.

As is apparent from this discussion, it is still uncertain how the modular organization of RFPs in auditory cortex is related to signal encoding and processing. More specifically, it is not clear whether different modules are an early expression of functional processing streams (Rauschecker and Tian 2000) or reflect general properties of stimulus representation and information distribution. In visual cortex, interpretation of the functional role of modular organization may seem to be contextual interaction or context-dependent comparison (Kas et al. 1997; Stettler et al. 2002); however, the modular organization could be interpreted as a byproduct of efficient synaptic connections and neural development (Adams and Horton 2003; Purves et al. 1992; Weinberg 1997).

Thalamic origins for receptive field parameters in AAF

RFPs of cat AI neurons are often directly inherited from those of thalamic neurons or are constructed by the convergence of outputs from several neurons in the MGB (Miller et al. 2001). Binaural properties in AI are also shaped by specific thalamocortical projections (Middlebrooks and Zook 1983; Velenovsky et al. 2003). Therefore it is appropriate to consider the contribution of thalamocortical projections to RFPs in AAF.

AAF has 2 major sources in the MGB and receives approximately 75% of the thalamocortical projections from the tonotopically organized ventral division and rostral pole (or the lateral part of the posterior group) of the MGB. The remaining nearly 25% of the thalamocortical projections to AAF originate from the nontonotopic dorsal and medial divisions of the MGB. These convergent inputs from different thalamic sources may create RFP distributions specific to AAF. The rostral pole of the MGB has been shown to have sparse CF representation between 1 and 5 kHz and an overrepresentation of the high-frequency range (Imig and Morel 1985b), which corresponds to the distorted CF representation observed in AAF. However, the sharp-tuning property of the rostral pole neurons of the MGB is not consistent with the general broad-tuning property of AAF neurons, although the overall Q10 value range (~2–22) of the rostral pole neurons of the MGB matches that of AAF neurons (Imig and Morel 1985b; Phillips and Irvine 1982). The projections from more broadly tuned neurons in the

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Factor 1</th>
<th>Factor 2</th>
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<tr>
<td>Threshold</td>
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</tr>
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<td>Q40</td>
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</tr>
<tr>
<td>Latency</td>
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<td>0.46</td>
</tr>
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The varimax orthogonal transformation was performed for receptive field parameter (RFP) residuals. Bold type represents the high correlation value for each RFP.
dorsal or medial divisions of the MGB (Calford 1983) may contribute to the broad-tuning property of AAF neurons. It might also be related to anatomical connections that span a broad frequency range within AAF (Lee et al. 2004). However, differences in strength of excitatory and inhibitory synaptic inputs relative to spiking threshold may also contribute to the

FIG. 9. Comparison of receptive field parameters between AAF (n = 74) and AI (n = 106) obtained from the same hemisphere (case 111L). Six units at the border were included in both areas. Mann–Whitney U test was performed for comparison. A: CF. Because RFPs in AAF are CF-dependent, the CF range for AAF was adjusted for AI. There was no significant difference in CF. B: threshold. AAF units had slightly lower threshold than AI units (P < 0.05). C: Q10. D: Q40. AAF units were significantly more broadly tuned than AI units (Q10: P < 0.0001, Q40: P < 0.001). E: latency. There was no significant difference for latency.

FIG. 10. Comparison of RFPs between AAF and AI from 7 and 16 hemispheres, respectively. RFPs were compared in an octave CF bin from 1 to 64 kHz. Box plots illustrate medians (horizontal lines), quartiles (box heights), and 10th and 90th percentiles (whiskers). Mann–Whitney U test was performed for statistical significance, illustrated by asterisks. *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001. Numbers in top panel indicate sample size for each group.

broad spectral bandwidth of spiking response (Tan et al. 2004; Wehr and Zador 2003). Latencies in the low- to mid-CF range of AAF are shorter than AI. Because there has been no direct comparison of the latency between the ventral division and rostral pole of the MGB neurons, both of which have relatively short latency
Comparative aspects of mammalian AAF

A tonotopic field anterior to AI, and thus a candidate for a field homologous to cat AAF, has been described in the mouse (Stiebler et al. 1997), the rat (Rutkowski et al. 2003), the gerbil (Thomas et al. 1993), the chinchilla (Harel et al. 2000; Harrison et al. 1996), the ferret (Shamma et al. 1993), an FM-bat (Esser and Eiermann 1999), the owl monkey (Imig et al. 1977), and the macaque monkey (Merzenich and Brugge 1973; Morel et al. 1993). In several species, RFP differences similar to the one described here for AAF and AI have been observed (Kowalski et al. 1995; Linden et al. 2003; Rutkowski et al. 2003). However, in some species, the observed differences do not match the pattern found in the cat. For example, in the chinchilla, AAF has longer latencies than those of AI (Harel et al. 2000; Harrison et al. 1996), and in the mouse, AAF and AI have similar bandwidth at 10 dB above threshold (Linden et al. 2003). It is not clear whether these differences result from some evolutionary or ethological differences or whether they are based on sampling biases.

In gerbil AAF, underrepresentation of low- to mid-frequency range has also been observed (Thomas et al. 1993). The underrepresented CF range is similar to the one described in this study and corresponds to the most sensitive frequency range (CF range with low threshold) of the peripheral auditory system for the animals (Liberman 1978; Ohlemiller and Echelter 1990). The underrepresented CF range could be related to temporal or spectral aspects generally considered relevant in sound localization and may thus explain that AAF may not be important for sound localization (Lomber and Malhotra 2003).

In the macaque auditory cortex, it has been proposed that there are 2 functionally different sound pathways for sound identification and location (Rauschecker and Tian 2000; Romanski et al. 1999; Tian et al. 2001). Two tonotopically organized lateral belt areas project to different areas of the prefrontal cortex (Romanski and Goldman-Rakic 1999; Romanski et al. 1999). The caudalateral or the anterior lateral area in the lateral belt field may be more sensitive to auditory space or monkey vocalization information, respectively (Tian et al. 2001). A similar segregation may exist in cat auditory cortex. In behavioral experiments, bilateral deactivation of AAF with cryoloops disrupted a performance in a temporal pattern discrimination task, but did not affect a performance in a sound-localization task (Lomber and Malhotra 2003). By contrast, cooling of the posterior auditory field showed disruption of a performance in a sound-localization task but not in a temporal pattern discrimination task (Lomber and Malhotra 2003). The shorter latencies, shorter receptive field durations (shorter integration time window), and higher repetition-frequency following property in AAF (Imaiizumi et al. 2003; Linden et al. 2003; Schreiner and Urbas 1988) support the idea that this field may be involved in processing of temporal structure necessary, for example, in the analysis of vocalization. Therefore it is conceivable that the functional differences between anterior and posterior cortical areas may reflect similar task-related parallel pathways as proposed for the monkey auditory system.

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References


