

Spectral and Temporal Processing in Rat Posterior Auditory Cortex

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The rat auditory cortex is divided anatomically into several areas, but little is known about the functional differences in information processing between these areas. To determine the filter properties of rat posterior auditory field (PAF) neurons, we compared neurophysiological responses to simple tones, frequency modulated (FM) sweeps, and amplitude modulated noise and tones with responses of primary auditory cortex (A1) neurons. PAF neurons have excitatory receptive fields that are on average 65% broader than A1 neurons. The broader receptive fields of PAF neurons result in responses to narrow and broadband inputs that are stronger than A1. In contrast to A1, we found little evidence for an orderly topographic gradient in PAF based on frequency. These neurons exhibit latencies that are twice as long as A1. In response to modulated tones and noise, PAF neurons adapt to repeated stimuli at significantly slower rates. Unlike A1, neurons in PAF rarely exhibit facilitation to rapidly repeated sounds. Neurons in PAF do not exhibit strong selectivity for rate or direction of narrowband one octave FM sweeps. These results indicate that PAF, like non-primary visual fields, processes sensory information on larger spectral and longer temporal scales than primary cortex.

Keywords: cortical coding, frequency modulation, neural information processing, nonprimary cortex, repetition rate transfer function, temporal integration, tonotopic organization

Introduction

Sensory information in the brain is represented by the distributed activity of large numbers of neurons over many distinct regions. Different cortical fields exhibit response selectivities that appear to be related to the perceptual deficits associated with inactivation of these regions. The visual fields V4 and middle temporal (MT), for example, exhibit selectivity for color and motion, respectively, and inactivation of each region specifically interferes with color or motion discrimination (Felleman and Van Essen 1991; Lennie 1998). Similar distributed processing of sensory features has also been documented in the auditory cortex of echolocating bats. Focal inactivation of the FM-FM (frequency modulated) area impairs discrimination of target distance, whereas inactivation of Doppler-shift Compensated Frequency impairs frequency discrimination (Riquimaroux et al. 1991). These experiments suggest that functional segregation of different features serves as a general sensory processing strategy throughout the cerebral cortex (Kaas 1982).

With each successive stage of sensory processing, neurons have a tendency to exhibit longer latencies, larger receptive fields, more adaptation to repeated stimuli, and less precise topographic representation of the sensory epithelium (Mountcastle 1997). For example, V2 neurons have larger receptive fields and longer onset latencies compared with V1

(Levitt et al. 1994; Schmolesky et al. 1998). The increases in classical receptive field size and longer latencies in the hierarchy of the visual cortex are accompanied by selectivity for more complex attributes of the visual scene. The mammalian auditory cortex appears to be organized in a similar manner. Neurons in cat AII typically exhibit broader frequency tuning, higher response thresholds, and less precise tonotopy than A1 neurons (Schreiner and Cynader 1984). The maximum following rate in response to temporally modulated stimuli of neurons in AII, posterior auditory field (PAF), and ventral PAF (VPAF) of cats is considerably slower than neurons in A1 and anterior auditory field (AAF) (Schreiner and Urbas 1988). Collectively, these studies indicate that higher order cortical areas analyze and integrate sensory information on larger spatial and longer temporal scales (Van Essen et al. 1992; Ehret and Romand 1997).

The rat offers many advantages for exploring the functional segregation of the nervous system. There is extensive knowledge of its cyto- and myelo-architecture (Winer and Larue 1987; Roger and Arnault 1989; Arnault and Roger 1990; Clerici and Coleman 1990; Romanski and LeDoux 1993; Shi and Cassell 1997; Winer et al. 1999; Kimura et al. 2003; Hazama et al. 2004). On the basis of thalamocortical projections, the auditory cortex of rat is anatomically subdivided into a central core region designated as TE1 and surrounding belt or secondary regions labeled TE2 and TE3 (Malmierca 2003). These differences in connectivity presumably provide a substrate for differences in information processing of spectral and temporal features of sounds. In addition, previous studies have documented rat psychophysical performance on a number of auditory tasks including frequency discrimination (Syka et al. 1996; Talwar and Gerstein 1998), gap detection (Ison et al. 1991; Syka et al. 2002), sound localization (Kelly and Kavanagh 1986), and modulation rate detection (Sakai et al. 1999). The rat has also been used extensively in cellular- and systems-level studies of cortical plasticity (Bakin and Weinberger 1996; Glazewski 1998; Kleim et al. 1998; Polley et al. 1999; Feldman 2000; Lebedev et al. 2000; Sachdev et al. 2000; Shulz et al. 2000; Ego-Stengel et al. 2001; Talwar and Gerstein 2001; Wallace et al. 2001; Desai et al. 2002).

Although auditory processing in the ascending auditory pathway has been extensively studied in the rat, relatively little data is available regarding the functional specialization of nonprimary fields. Although electrophysiological studies have generally focused on response characteristics of primary auditory cortex neurons (Horikawa et al. 1988; Sally and Kelly 1988; Thomas and Tillein 1997; Kilgard and Merzenich 1999), considerable evidence suggests the existence of a functionally distinct PAF (Zhang et al. 2001; Doron et al. 2002; Rutkowski et al. 2003). The purpose of this study is to compare spectral and temporal processing in the primary and PAFs. Given the lack of

understanding of the functional roles of the nonprimary fields, the importance of systematically quantifying spectral and temporal response properties of auditory cortical neurons is a crucial first step in determining the role of these fields in acoustic processing.

Materials and Methods

Surgical Preparation

Dense microelectrode mapping techniques were used to collect data from 379 microelectrode penetrations into the right auditory cortex of 9 adult female Sprague-Dawley rats (250–325 g). Methods were similar to those described in previous publications from this lab (Kilgard, Pandya, Vazquez, Gehi et al. 2001; Engineer et al. 2004; Moucha et al. 2005). All protocols and recording procedures conformed to the Ethical Treatment of Animals (National Institutes of Health, NIH) and were approved by the University Committee on Animal Research at the University of Texas at Dallas. Animals were anesthetized with sodium pentobarbital (50 mg/kg). Supplemental pentobarbital (8 mg/mL) was periodically administered either subcutaneously or intraperitoneally to maintain a state of are flexia throughout the surgical procedures and during the recording session. The trachea was cannulated and humidified air was provided to ensure adequate ventilation and to minimize breathing related noises. After a surgical level of anesthesia was obtained, the skull was fixed in a palato-orbital restraint and exposed through a rostrocaudal incision. The cisternae magna was drained of cerebrospinal fluid to minimize cerebral edema. The temporalis muscle was reflected and the dura over the right auditory cortex was exposed through a craniotomy of approximately 6 by 4 mm. The dura was resected and the cortex was maintained under a layer of viscous silicone oil to prevent desiccation. A digitized image of the cortical surface was taken to aid in electrode placement and topographic reconstruction. The electrocardiogram and a pulse oximeter were used to monitor circulatory function and to control the depth of anesthesia. Body temperature was monitored with a rectal probe and maintained at 37°C with a heating pad (FHC, Bowdoin, ME). Proper hydration was maintained with lactated Ringers solution provided periodically during the course of the acute experiment.

Action potentials were recorded simultaneously from 2 Parylene-coated tungsten microelectrodes (FHC, 2 M Ω at 1 kHz) glued together (250 μ m separation) and lowered into the cortex using a micromanipulator (FHC). The insertion was orthogonal to the cortical surface. Recordings were made at a depth of approximately 550–650 μ m, corresponding to layers IV/V in both A1 and PAF. Tucker-Davis Technologies (Alachua, FL) neurophysiology hardware (DB4, AP2, AD2, and DA3/4) and software (Brainware) were used for signal filtering (0.3–8 kHz), amplification (10 000 \times), data acquisition, and stimulus generation. Potentials above approximately 0.18 mV were considered to be action potentials. Whenever this fixed threshold was exceeded, action potential waveforms were recorded for more detailed quantitative analysis. Neural responsiveness was quantified using multiunit data. Recordings were derived from 10 to 60 recording sites in each animal over the course of each 8- to 34-h experiment. Penetration sites were chosen to avoid damaging blood vessels while generating a detailed and evenly spaced map.

Acoustic Stimulation and Recording

Recordings were made in a shielded, doubled-walled sound chamber (Acoustic Systems, Austin, TX), and sounds were presented in the free-field using a calibrated speaker. Frequency and intensity calibrations were performed with an ACO Pacific microphone (PS9200-7016) and Tucker-Davis SigCal software. The speaker (Motorola model # 40-1221) was positioned directly opposite the contralateral ear at a distance of 10 cm. Tucker-Davis Technologies hardware and software (SigGen) were used for stimulus generation. Tone amplitudes were calibrated for every frequency presented and digitally adjusted to ensure that intensities were flat from 1 to 32 kHz. Auditory frequency response tuning curves (spectral receptive fields) were determined by presenting tones of 81 different frequencies (logarithmically spaced from 1 to 32 kHz) at each site. Each frequency was presented at 16 intensities ranging between

0 and 75 dB SPL (1296 total stimuli). Tuning curve tones were randomly interleaved and separated by at least 475 ms between presentations to minimize adaptation effects. All tones had 5 ms rise and fall times (cosine squared gated) and were 25 ms in total duration.

To determine temporal selectivity to periodic stimuli, repetition rate transfer functions (RRTF) in response to tones and noise bursts were derived at each site by presenting a series of tone and noise burst trains. The carrier frequency of the tone trains was one of 8 frequencies (1.3, 2, 3, 5, 9, 14, 19, or 29 kHz, whichever was nearest to the site's BF) presented in sets of 6 tone bursts (25 ms each at 70 dB) at 14 repetition rates ranging from 3 to 19 Hz. Although these tone trains were excluded if a best frequency (BF) could not be determined, all sites received tone trains of 5 and 12 kHz presented at 10 Hz and 75 dB. The responses to 5 and 12 kHz tones were used to quantify the population response to tones of nonoptimal frequency. Noise bursts trains contained 6.75-dB noise bursts (each noise burst was 1.2–30 kHz bandwidth) presented at repetition rates of 5, 10, 15, and 20 Hz. Twelve repetitions of each train were presented in random order. Because 2 s of silence precede each train, we consider the first onset to be representative of a train presented at 0.5 Hz.

Responses to 12 FM tones (3 rates \times 2 octaves \times 2 directions) were recorded from A1 and PAF neurons. Each FM sweep spanned a single octave. Three different sweep durations were presented: 40, 160, and 640 ms (corresponding to 25, 6.25, and 1.56 oct/s). The starting frequency of each sweep was always 1, 2, 4, 8, 16, or 32 kHz. At each site, upward and downward sweeps spanning the octave above and the octave below the BF were presented. For example, if a site had a BF of 3.5 kHz, both 2–4 kHz and 4–8 kHz sweeps were presented. At broadly tuned sites without a clear BF, 4–8 kHz and 8–16 kHz FM sweeps were presented. FM stimuli were randomly interleaved. A silent interval of at least 1 s occurred between each FM sweep to minimize adaptation effects. Twenty repetitions of each FM stimulus were presented.

Data Analysis

MATLAB (Mathworks, Natick, MA) was used for all analysis. To prevent the possibility of experimenter bias, an experienced blind observer determined tuning curve parameters. The parameters were defined by hand using custom software that displayed raw action potential data without reference to the frequencies and intensities that generated the responses, the penetration location, or the identity of the animal. For each site, the BF, threshold, bandwidth (10, 20, 30, and 40 dB above threshold), and latency data were recorded. Figure 1 provides an example of representative tuning curves from A1 and PAF and the parameters derived from each, including threshold and bandwidth. The BF was defined as the frequency where a response is obtained to the lowest stimulus intensity (i.e., threshold). Individual maps were considered to be tonotopically organized if they exhibited a significant relationship (correlation coefficient) between BF (in octaves) and anterior–posterior position. To test the possibility that PAF is tonotopically organized along a direction other than anterior–posterior, we also examined the relationship of BF and position along the dorsal–ventral axis (and every other possible orientation).

Bandwidth was defined as the frequency range (in octaves) that activated the neurons at 4 intensity levels above threshold. Examples of poststimulus-time histograms (PSTH) for multiunit clusters from A1 and PAF are shown below each representative tuning curve. Peak latency was quantitatively determined as the time to reach peak response in the PSTH (1-ms bins) formed from the responses to all tones within each site's excitatory receptive field. The onset and end-of-peak latencies were the times after stimulus onset at which activity exceeded and fell below 2 standard deviations over the spontaneous activity level, respectively.

The function relating firing rate and tone intensity was determined using the average response to all tones within each site's receptive field. Responses were considered nonmonotonic if there was a significant negative correlation ($P < 0.01$) between tone intensity and the average number of action potentials in response to tones at each of the intensities above the intensity that generated the maximum response.

The rate-based modulation transfer function was the average number of responses (above background) occurring within a fixed analysis window following the second through sixth sounds of each train as

a function of repeat rate. The analysis windows used for each region were based on the interval after each sound when the population PSTH of all sites from that region was significantly ($P < 0.05$) above background activity (to avoid contamination from epochs of reduced background activity). For A1, the window was from 11 to 35 ms. For PAF, the window was from 14 to 85 ms. For PAF, the analysis windows would have overlapped at rates above 14 Hz. At those rates, the number of evoked action potentials per sound was simply the number of driven action potentials (i.e., above background) between 14 ms after the second tone and 85 ms after the sixth tone divided by 5. Best modulation rate (BMF) is the repetition rate that evoked the maximum number of action potentials per sound. Limiting rate is the maximum repetition rate with more than half the response at the BMF. Dot rasters of representative A1 and PAF responses to stimulus tone trains of varying repetition rates are shown in Figure 9.

The responses to tone and noise burst trains were also quantified using vector strength (VS) (Goldberg and Brown 1969) and Rayleigh statistic measures (Lu and Wang 2000; Liang et al. 2002). VS quantifies the degree of synchronization between action potentials and repeated sounds, and the mean VS is calculated with the formula:

$$\bar{R} = \frac{1}{n} \sqrt{x^2 + y^2} = \frac{1}{n} \sum_{i=1}^n \cos \theta_i, y = \frac{1}{n} \sum_{i=1}^n \sin \theta_i, \theta_i = 2\pi \frac{t_i}{T}$$

where n = total number of action potentials, t_i is the time of occurrence of the i th action potential, and T is the interstimulus interval. Perfect synchronization would result in a value of one, whereas no synchronization would result in a value of zero. Rayleigh statistic ($2nVS^2$, where n is the total number of action potentials) is a circular statistic that combines the previous 2 measures to assess the statistical significance of the VS (Mardia and Jupp 2000). Values greater than 13.8 indicate statistically significant ($P < 0.001$) phase locking.

Differences in FM responses were quantified by computing the average population PSTH of each field in response to a one octave sweep, and the direction selectivity (DS) of individual recording sites using a standard metric (Mendelson et al. 1993; Shamma et al. 1993; Heil

and Irvine 1998b; Tian and Rauschecker 2004). The DS metric was defined using the following index:

$$DS = (R_{up} - R_{down}) / (R_{up} + R_{down})$$

R is the response (in number of action potentials per 20 repetitions) elicited by the upward or downward FM sweep. A DS value of 0 indicates no preference for either sweep direction, whereas a value of +1 or -1 indicates complete preference for the upward or downward direction, respectively. The degree of DS was determined by calculating the absolute value of the DS index. Action potentials occurring from 8 ms after the beginning and 50 ms after the end of each sweep were analyzed. Spontaneous activity, calculated as the average firing rate during the first 8 ms before a driven response, was subtracted. Only sites with a driven response of at least 0.5 action potentials per stimulus to one or more of the FM sweeps were analyzed.

To quantify how increasing the duration of one octave FM sweeps alters the response of A1 and PAF neurons, we subtracted the average number of action potentials occurring within 690 ms of FM onset for 640 versus 160 ms sweeps and for 160 versus 40 ms sweeps. The sweeps with the frequency range and direction that evoked the maximum number of action potentials at each site were used for this analysis. To test whether neurons in A1 and PAF respond more strongly to FM sweeps compared with tones, we subtracted the average number of action potentials evoked in the first 200 ms from sound onset in response to a 25-ms tone from the response to a 160 ms one octave FM sweep. The tone frequency and FM range were selected to maximally activate each site.

A1 was functionally defined on the basis of latency and tonotopy (as in Kilgard and Merzenich 1999). In general, sites with minimum latencies less than 20 ms were classified as A1 sites. Only 4% of A1 sites in this study exhibited longer latencies. The Voronoi tessellation procedure (MATLAB, Mathworks) was used to visualize the topography of A1 and PAF (as in Kilgard and Merzenich 1998). The boundaries of the cortical map were either the limits of data collection or sites nonresponsive to auditory stimuli.

Because PAF neurons rarely exhibited extremely high or low best frequencies (Fig. 2) and bandwidth and threshold are known to vary with BF, statistical analyses were conducted on populations of A1 and PAF recording sites with comparable frequency preferences to avoid overestimating the difference between A1 and PAF response properties. Specifically, we excluded 100 A1 sites and 11 PAF sites with BF either below 2 kHz or above 16 kHz. If these sites were not excluded, the

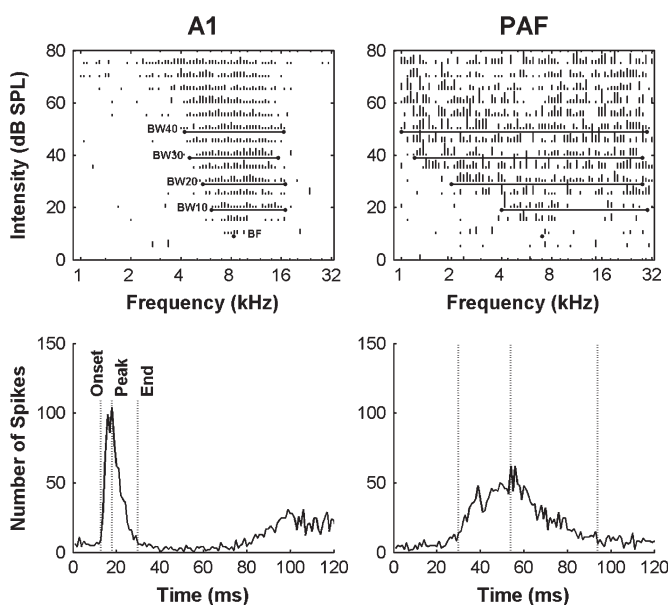


Figure 1. Representative tuning curves and PSTH from sites in primary auditory cortex (A1) and PAF. For each tuning curve, the length of each vertical line segment indicates the number of action potentials evoked by each tone. BF is the frequency that elicits a consistent neural response at the lowest intensity level (neural threshold). Bandwidth is the range of frequencies the neurons are responsive to at the specified intensity above threshold, expressed in units of octaves. PSTHs for both the A1 and PAF example are shown below each respective tuning curve. The relevant features derived from each PSTH are labeled (onset latency, peak latency, and end-of-peak latency).

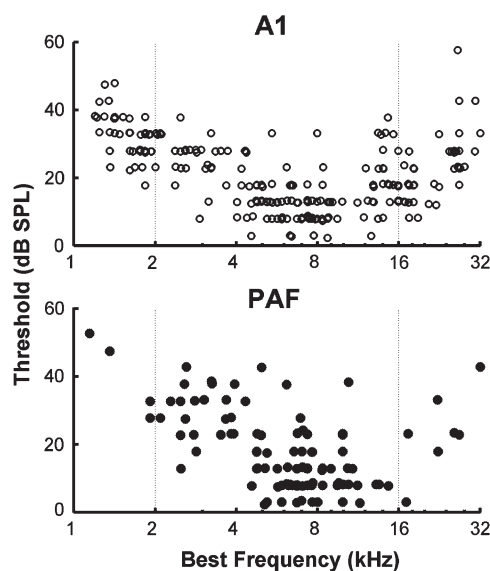


Figure 2. Neural thresholds to elicit excitatory responses at the BF for both A1 (top) and PAF (bottom) neurons sampled from 9 animals. The data points between the dotted vertical lines at 2 and 16 kHz indicate the sites that were included for statistical analysis of receptive field and temporal properties.

differences in bandwidth between the fields would have been (artificially) larger than reported below (data not shown), and the mean A1 response threshold would have been (artificially) higher than PAF. The data set used to determine bandwidth and latency contained 173 A1 sites from 9 animals and 95 PAF sites from 5 animals.

Statistical analysis was done using MATLAB. Two-tailed Student's *t*-tests were used to establish the statistical significance of each difference of response characteristics across the 2 fields. Paired Student's *t*-tests were used to determine the statistical significance of response facilitation in A1 and adaptation in PAF, and increasing numbers of evoked action potentials with increasing FM duration. The error bars on all figures reflect standard error of the mean.

Results

General Observations

Frequency-intensity tuning curves in both PAF and A1 had broader bandwidths as intensity increased (Fig. 1). Most recording sites in A1 and PAF exhibited monotonic rate level functions (A1: $85 \pm 4\%$; PAF: $95 \pm 4\%$, $P = 0.08$). Responses from A1 and PAF showed similar intensity thresholds ($P > 0.5$), which increased near the extremes of the hearing range (Fig. 2). A representative BF map of A1 and PAF for one animal is shown at the top of Figure 3. The BF of A1 neurons increased from posterior to anterior (Sally and Kelly 1988; Kilgard and Merzenich 1999; Doron et al. 2002; Rutkowski et al. 2003) (Fig. 4). All 9 A1 maps exhibited strong and significant correlations between anterior-posterior location and BF ($R = -0.85 \pm 0.04$, $P < 0.0000001$). No consistent correlation was observed in the PAF maps ($R = 0.09 \pm 0.24$, $P > 0.5$). BF was not significantly correlated with anterior-posterior position in 3 out of 5 maps and the remaining 2 were in opposite directions. To test the possibility that PAF is topographically organized in a direction other than anterior to posterior, we also examined the best correlation between frequency and location at all the other possible orientations. For A1 sites, using the best orientation slightly improved the relationship between frequency and location ($R = -0.87 \pm 0.02$, $n = 9$, $P < 0.0000001$). For PAF sites, the average correlation was not significant ($R = 0.15 \pm 0.23$, $n = 5$, $P > 0.5$) even when evaluated in this less restrictive manner.

Receptive Field Size (Bandwidth)

One of the most pronounced differences between A1 and PAF is the broader excitatory bandwidths of PAF neurons (Fig. 5). Receptive field sizes in PAF were on average over 65% wider than A1 neurons. The 10th and 90th percentiles for A1 bandwidth at 10 dB above threshold were 0.52 and 1.85 octaves, respectively, whereas they were 0.81 and 2.96 octaves for PAF neurons. At 30 dB above threshold, the 10th and 90th percentile values were 1.01 and 3.37 for A1 and 2.38 and 4.63 octaves for PAF neurons. The sharp transition in the excitatory bandwidth at the A1-PAF border of an individual animal is shown in the middle plot of Figure 3. For instance, the 1.2 kHz A1 recording site and the neighboring 7 kHz PAF site were separated by only 200 μm and yet their bandwidths differed by a factor of 4.

Longer Response Latency in PAF Compared with A1

Measures of response latency also show significant differences between A1 and PAF neurons. All latency measures revealed that PAF neurons were longer and more variable in latency than A1 sites. Neurons in A1 typically respond with a narrow burst of action potentials 10–35 ms after sound onset (Fig. 1—bottom

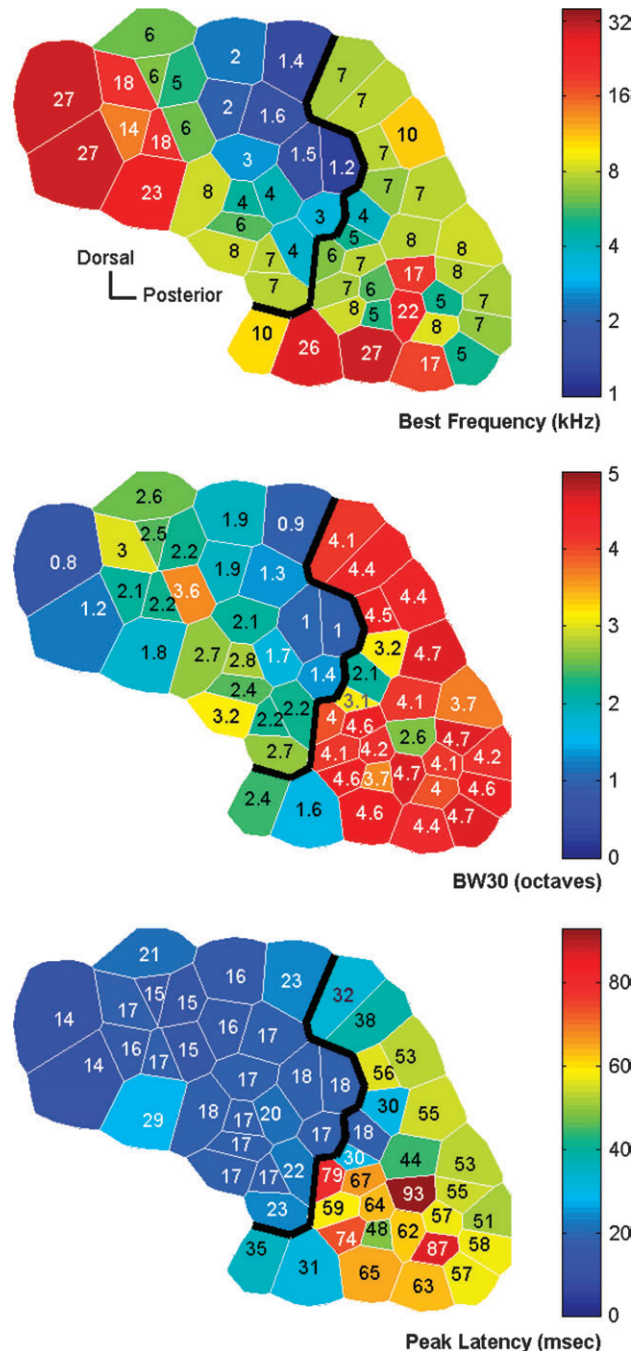


Figure 3. Representative map of BF (top), bandwidth 30 dB above threshold (middle), and peak latency (bottom) in A1 and PAF from one animal. Each polygon represents one microelectrode penetration. The number within each polygon indicates the value for each respective response parameter. The dark black line bisecting the polygons in all 3 maps indicates the separation between A1 and PAF sites. In the top panel, color represents each site's BF in kilohertz. In this example, note the orderly progression of BF in A1 and a breakdown in PAF tonotopy. In the middle plot, color represents the bandwidth 30 dB above threshold. The considerably wider excitatory receptive field size of PAF sites was one of the criteria used to confirm the A1-PAF border. In the bottom panel, color represents the peak latency of each site derived from the tuning curve PSTH. The substantially longer response latency of PAF neurons is an additional criterion that was used to distinguish A1 from PAF sites. The line length on the direction marker shows the scale (125 μm).

left). PAF neurons, on the other hand, typically respond with action potentials from 35 to 90 ms after sound onset (Fig. 1—bottom right). The onset latency, latency to the peak of

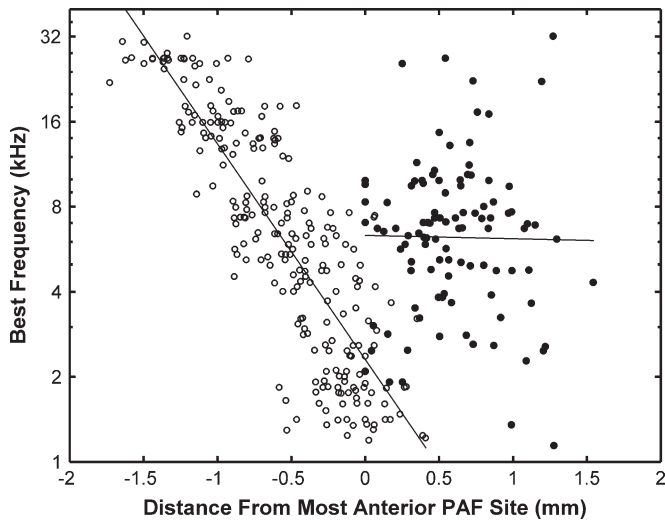


Figure 4. Tonotopic organization is maintained in A1, but not in PAF. This scatter plot shows the relationship between anterior-posterior location and BF for each A1 (open circles) and PAF (filled circles) recording site. Positive distances are posterior to the most anterior PAF site. Lines denote the linear regression functions for A1 and PAF sites, respectively. Individual rats exhibited a strong relationship of frequency in the anterior-posterior axis, whereas PAF neurons exhibited no consistent topography from anterior to posterior.

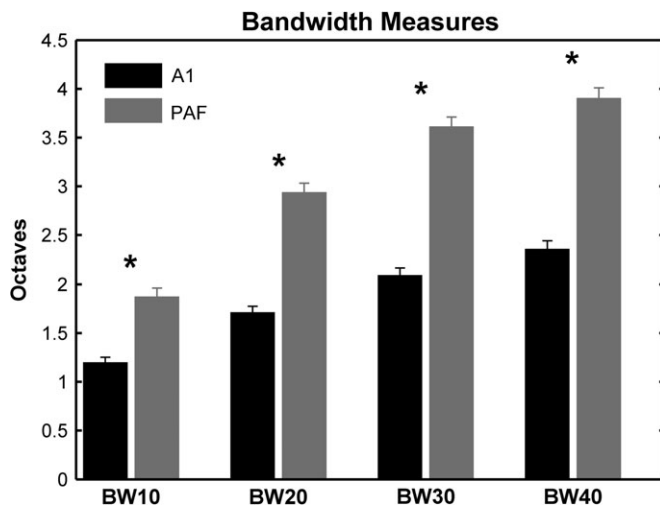


Figure 5. Average receptive field sizes of PAF neurons are wider than A1 neurons. Bars plot the mean bandwidths at 4 intensities above threshold (dB) for A1 (black) and PAF (gray) neurons with BFs between 2 and 16 kHz. Bandwidth measures for A1 ($n = 149$ sites) and PAF ($n = 94$) sites were collected from 9 animals. All 4 average bandwidths were significantly wider in PAF than A1. *Statistical significance at $P < 0.0001$.

neuronal response, and termination of the cortical response were determined for each recording site. Average onset latencies, peak latencies, and end-of-peak latencies of units in PAF were 168, 165, and 153 percent longer, respectively (Fig. 6). Each of these 3 measures of response latency was significantly longer in PAF neurons and was used to confirm the A1-PAF border. The PAF peak latency standard deviation was more than twice that of A1 sites (31 vs. 12 ms).

The population PSTH in response to repeated 25 ms tone bursts presented at 5 and 12 Hz for both A1 ($n = 99$ sites) and PAF ($n = 87$ sites) neurons are shown in Figure 7; these illustrate

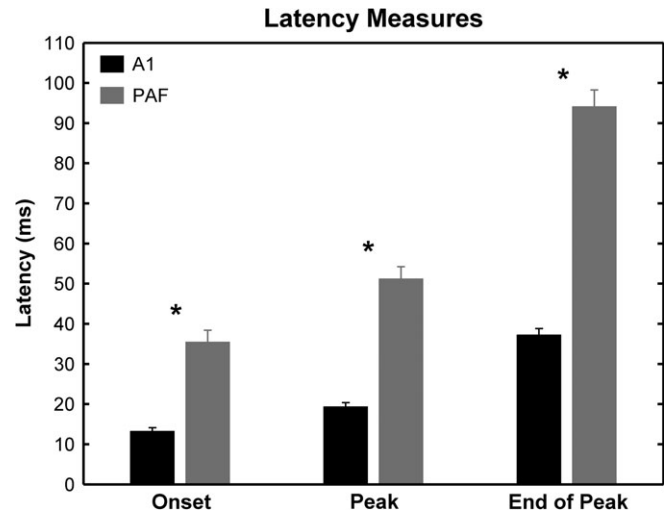


Figure 6. Average neural latencies of PAF neurons are longer than A1 neurons. Comparison of 3 different latency measures for A1 and PAF sites with BFs between 2 and 16 kHz. Latency measures for A1 ($n = 149$ sites) and PAF ($n = 94$) sites were collected from 9 animals. Asterisks indicate that all 3 latency measures were significantly longer in PAF than A1. *Statistical significance at $P < 0.0001$.

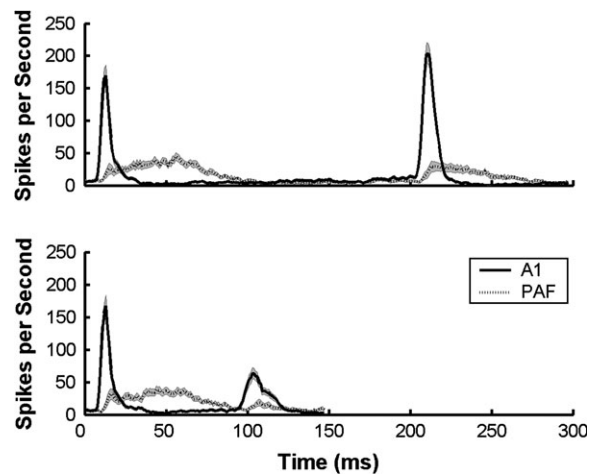


Figure 7. Population PSTH differences between A1 and PAF in time course and duration of activation in response to repetitive tonal inputs presented at BF. In the top panel, the population PSTH to 25 ms tones presented at 5 Hz (195 ms stimulus onset asynchrony (SOA)) shows facilitation in A1 that is not evident in PAF (see Fig. 10). In the bottom panel, the population PSTH to 25 ms tones presented at 12 Hz (82 ms SOA) shows adaptation in both fields. Gray patches indicate standard error of the mean. Note the considerable temporal lag and extended response duration of PAF sites.

the temporal lag and extended response duration of the PAF response. To illustrate the abrupt transition in stimulus-dependent response timing, a map of peak latency from an individual animal is shown in the bottom plot of Figure 3.

Comparison of Response Strength for Tonal and Broadband Stimuli

Earlier studies in primates and cats have suggested that although A1 neurons prefer tones, some nonprimary fields prefer sounds with a broader spectral profile (Rauschecker et al. 1995; Rauschecker 1998a). To test this hypothesis in rat PAF, we quantified the average number of action potentials evoked by broadband white noise and tones at each recording site (Fig. 8).

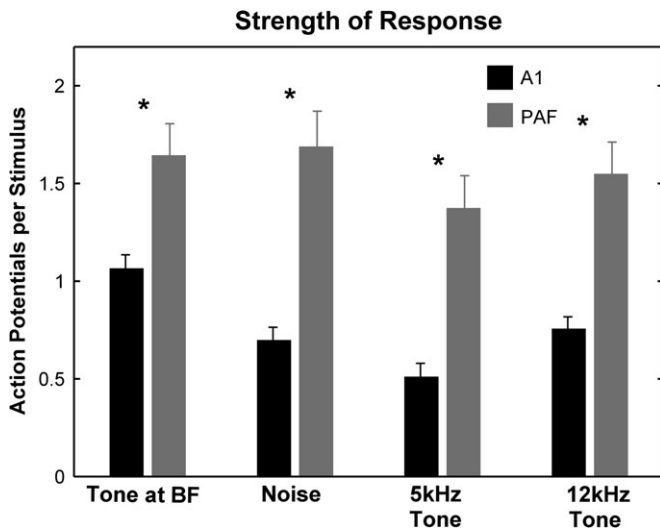


Figure 8. Average response strength to tones and noise bursts in A1 and PAF neurons. The number of action potentials per stimulus for A1 ($n = 142$ sites) and PAF ($n = 86$) sites with BFs between 2 and 16 kHz were collected from 9 animals. These results demonstrate that both narrowband and broadband sounds generate more robust responses in PAF than in A1. *Statistical significance at $P < 0.0005$.

PAF neurons responded with more action potentials to both types of sound. Although A1 responded to BF tones with significantly more action potentials than any of the 3 other sounds, PAF responses did not significantly differ across the sounds presented. This difference may result from the wider bandwidths of PAF neurons described above. The PAF population response to any particular tone frequency (i.e., 5 or 12 kHz presented at 75 dB) was 50–75% greater than A1 because of the broader receptive field size of PAF neurons.

Comparison of Temporal Following Properties in A1 and PAF

Because natural sounds typically contain important time-varying information, it is important to understand how primary and nonprimary auditory cortex neurons represent this information. Although the behavioral and perceptual consequences of differences in the encoding of temporal information for different fields are at present unknown, previous investigations showed significant differences in the temporal following capacities of cat auditory cortical fields (Schreiner and Urbas 1988; Eggermont 1998). To test if similar differences are present in rat auditory cortex, responses to modulated trains of tones and noise bursts were quantified in PAF and A1.

Earlier reports have shown that most A1 neurons act as low pass filters and respond with fewer action potentials per tone when stimulated by tones trains at rates above 10 Hz (Gaese and Ostwald 1995; Kilgard and Merzenich 1999; Orduna et al. 2001). Examples of A1 and PAF responses to tone and noise burst trains are shown as dot rasters in Figure 9. To quantify differences in response adaptation between the 2 fields, we determined the mean repetition rate transfer function (RRTF) for both A1 and PAF sites (Fig. 10). The average limiting repetition rate (50% of response at the best repetition rate) for A1 neurons was 7.2 ± 0.2 Hz compared with 1.6 ± 0.4 Hz for PAF neurons ($P < 0.000001$). In other words, PAF neurons require more than twice as long as A1 for the response to a second sound to recover to 50% of the response to the first. Peak latency was

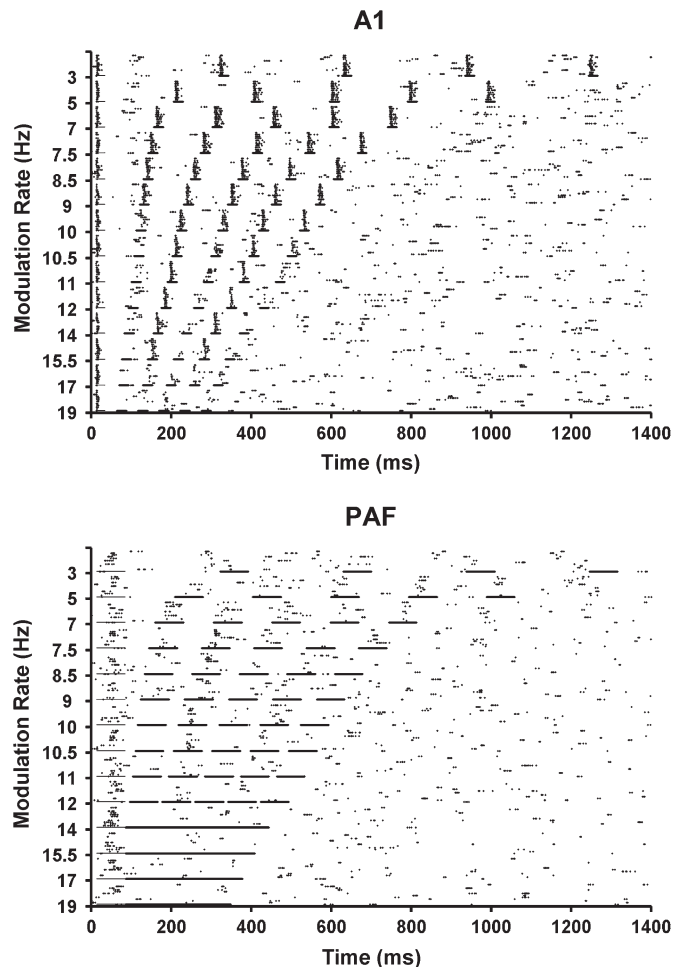


Figure 9. Individual examples of dot rasters from an A1 and a PAF site in response to trains of tones at different repetition rates. In general, the ability for individual sites to respond to each element decreased in both A1 and PAF as rate increased. In this example, the PAF site was slower to respond to stimulus onset and adapted to repeated stimuli (both tonal and broadband) at much slower repetition rates. The leftmost horizontal lines mark the time windows used to quantify the response to the first sound onset. The other horizontal lines indicate the windows used to calculate the neural response to the latter sounds (see Methods).

negatively correlated with limiting rates for both A1 ($R = -0.31$, $P < 0.05$) and PAF ($R = -0.34$, $P < 0.005$) neurons.

For rates between 4 and 8 Hz, A1 neurons exhibited significant facilitation in their responses to tones or noise bursts within these trains compared with the same sounds presented in isolation. For example, A1 neurons responded with 0.64 ± 0.06 (mean \pm standard error of the mean) more action potentials per stimulus to 5 Hz modulated tones compared with the same tone presented in isolation ($P < 0.0001$). For 5-Hz noise burst trains, A1 sites responded with 0.58 ± 0.05 additional action potentials per stimulus ($P < 0.00001$). The average A1 response per stimulus was significantly decreased at rates above 10 Hz for both tones and noises.

Neurons in PAF rarely exhibited facilitation to repetitive tones or noise bursts and exhibited significant response adaptation at rates above 4 Hz. For example, PAF neurons responded with 0.71 ± 0.11 fewer action potentials per stimulus for 5 Hz modulated tones compared with the same tone presented in isolation ($P < 0.01$). For repeated noise bursts, PAF neurons responded with 0.71 ± 0.09 fewer action potentials

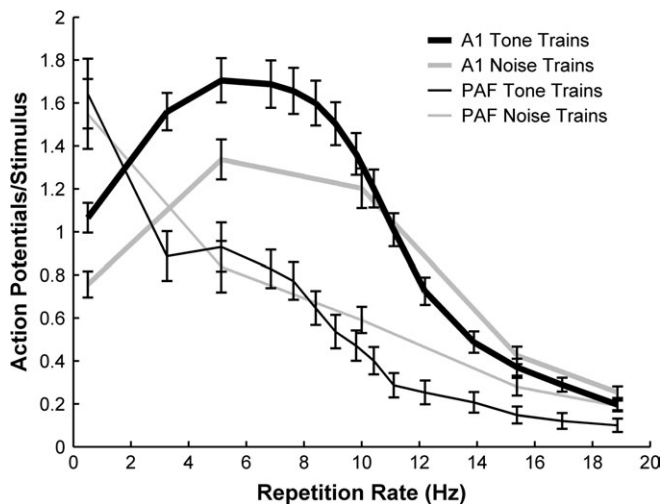


Figure 10. The mean RRTF for tones and noise in A1 and PAF sites. The number of evoked action potentials per tone or noise burst at each repetition rate is plotted with standard error of the mean for sites with BFs between 2 and 16 kHz. For both A1 and PAF neurons, the shape of the function was similar for tones and noise bursts. The maximum cortical following rate evoked by a train of sounds reliably fell off at a repetition rate of ~10 Hz for A1 neurons (as in Kilgard and Merzenich 1999) and at a rate above 5 Hz for PAF neurons. It should be noted that many individual A1 and PAF sites exhibited significant structure not evident in the mean repetition rate transfer function. The mean repetition rate transfer function for A1 ($n = 142$ sites) and PAF ($n = 86$) sites was collected from 9 animals.

per stimulus at 5 Hz ($P < 0.00005$). The stronger adaptation, longer latency, and extended response duration of PAF neurons compared with A1 neurons can also be seen in the population PSTH of responses to tones pips with onsets separated by 195 or 82 ms (Fig. 7).

Responses to tone and noise burst trains are significantly better synchronized in A1 compared with PAF at rates above 5 Hz (Fig. 11). As a population, A1 VS is highest at 9 Hz, whereas PAF is highest at 5 Hz. The average maximum VS in response to tone trains is 0.89 ± 0.01 for A1 neurons and 0.70 ± 0.02 for PAF ($P < 0.000001$). The average maximum Rayleigh statistic in response to tone trains is 241 ± 11 for A1 neurons and 113 ± 12 for PAF ($P < 0.000001$). Twice as many A1 sites exhibit significant phase locking compared with PAF at rates above 10 Hz (Fig. 11C). Thus, the observation of a progressive reduction of temporal resolution at ascending levels of the auditory neuraxis continues through PAF in the rat (Langner 1992; Eggermont 2001; Joris et al. 2004).

Cortical Responses to FM Stimuli

Neurons in the PAF of cats exhibit selectivity for the rate and direction of FM sounds (Tian and Rauschecker 1998). To compare the degree of direction and rate selectivity in rat A1 and PAF, we recorded responses to one octave FM sweeps from a subset of our recording sites (A1: $n = 91$ sites from 6 rats; PAF: $n = 77$ sites from 5 rats). To illustrate the time course and duration of activation of each field, the average population PSTH for 160 ms FM sweeps recorded from A1 and PAF sites is shown in Figure 12. Although A1 neurons responded with more action potentials to the sweep compared with the tone, PAF neurons responded similarly to both. Although the 160 ms FM sweep evoked 0.78 ± 0.15 more action potentials in A1 than a short tone burst (presented at the BF) ($P < 0.0001$), neurons in

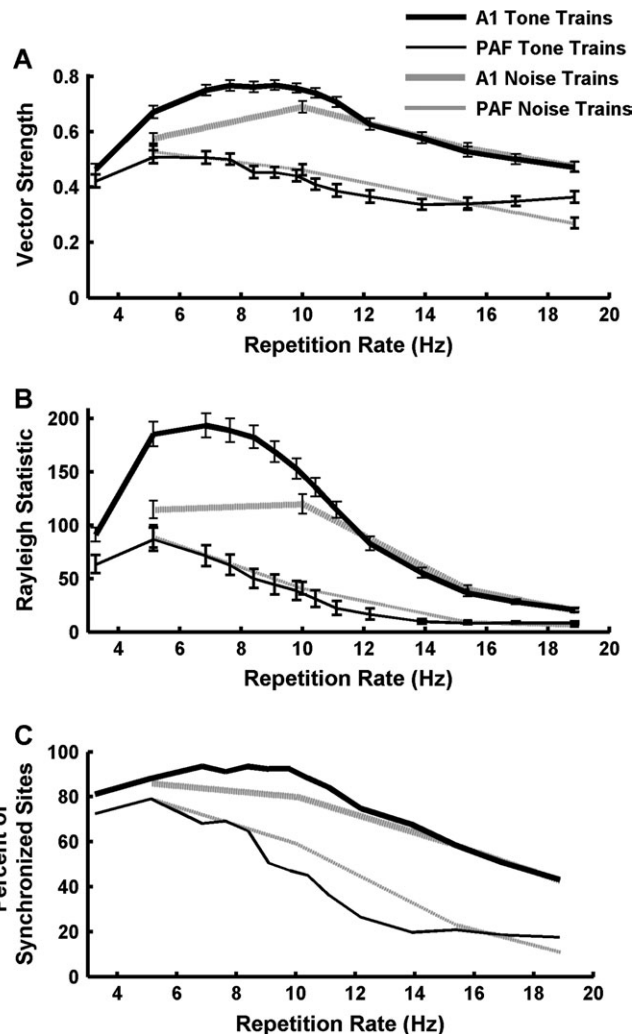


Figure 11. Synchronization of A1 and PAF responses to tone and noise burst trains. (A) Vector strength is a quantification of the degree of stimulus phase locking, where 1 would indicate every action potential arrives with the same latency relative to sound onset. (B) Rayleigh statistic is a confidence measure for the vector strength. Any number above 13.8 indicates significant ($P < 0.001$) phase locking. (C) Percent of synchronized sites at each repetition rate.

PAF responded with only 0.11 ± 0.16 additional action potentials ($P > 0.1$).

Our results indicate that PAF neurons are not particularly sensitive to the direction of these sounds. We quantified FM selectivity in both areas using a standard measure known as the FM DS index (see Methods). In Figure 13, mean firing rates in response to upward and downward FM sweeps and the distribution of the selectivity index for 40-, 160-, and 640-ms duration sweeps are presented. DS has a value of +1 for responses to only upward, but not downward FM sweeps, and -1 for responses only to downward FM sweeps, and zero for responses that are the same regardless of direction. For 160-ms duration sweeps, PAF has a preference for the downward direction ($P < 0.05$), whereas A1 shows no preference for upward or downward frequency sweeps. A1 neurons have approximately equal number of sites that are selective to upward and downward sweeps. As a result, the average degree of DS for 160-ms one octave sweeps (quantified as the absolute value of the DS index) is greater for A1 than PAF (A1: 0.24 ± 0.03

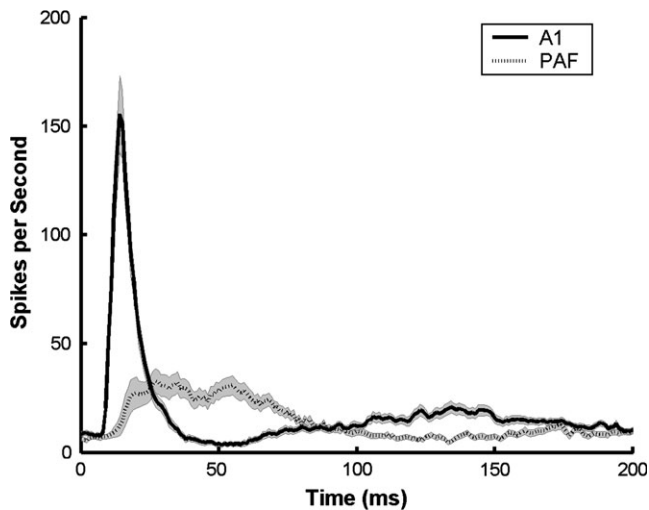


Figure 12. Population differences between A1 and PAF in time course and duration of activation in response to FM sweeps. This population PSTH shows the response from 91 A1 sites and 77 PAF sites (with BFs between 2 and 16 kHz) from a total of 6 animals to 160-ms upward FM sweeps. Note that A1 neurons exhibit additional activity (at ~150 ms) not seen in response to the tone presented in Figure 7. PAF neurons did not exhibit this additional response.

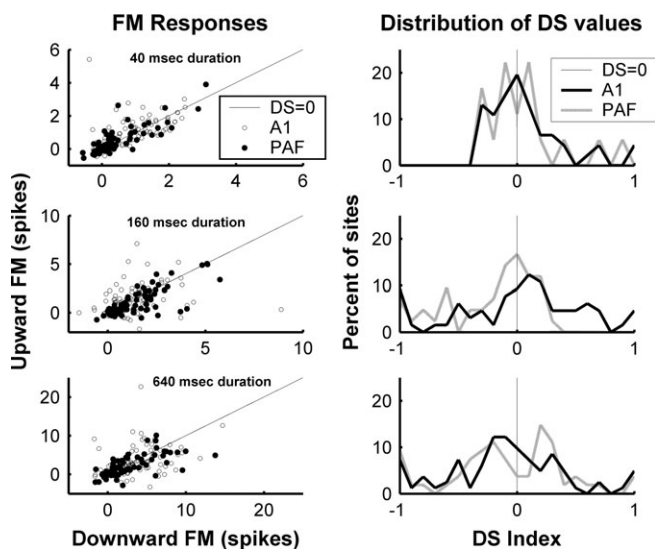


Figure 13. DS for one octave FM sweeps. In the left column, each scatter plot shows a comparison of the mean firing rates for each site in response to upward and downward FM sweeps with 40-, 160-, and 640-ms durations. The solid diagonal line represents a slope of 1. In the right column, each histogram shows the distribution of the DS values for each of the 3 FM durations (excluding sites that did not respond to either the upward or downward sweep with at least 0.5 spikes).

vs. PAF: 0.14 ± 0.02 , $P < 0.01$). Neither PAF nor A1 show a net preference for upward or downward FM sweeps that span one octave in 40 or 640 ms, and both fields exhibit equivalent degrees of DS at these rates. These results do not support the hypothesis that PAF neurons are strongly tuned for FM direction.

To determine whether A1 or PAF neurons are more strongly tuned to FM rate, we compared the responses of individual sites to 40-, 160-, and 640-ms duration FM sweeps. A1 neurons responded with 2.8 ± 0.4 additional action potentials to the 640-ms sweep compared with the 160-ms sweep ($P < 0.0005$). PAF

neurons responded with 1.2 ± 0.3 additional action potentials ($P < 0.0005$). A1 neurons responded to the 160-ms sweep with 1.0 ± 0.2 additional action potentials compared with the 40-ms sweep. In contrast, PAF neurons responded with only 0.2 ± 0.15 additional action potentials ($P > 0.1$). These results indicate that A1 and PAF neurons simply respond with more action potentials as FM sweep duration increases.

Discussion

Systematic exploration of nonprimary cortex using complex stimuli has been extremely useful in gaining insight into the central mechanisms of sensory processing. Many studies have found that neurons in distinct fields can be highly selective for certain sensory features and insensitive to others. For example, cortical areas beyond V1 and V2 show greater specializations for processing different attributes of the visual form (Livingstone and Hubel 1988; Bartels and Zeki 1998). In the mustached bat, a species in which the key information bearing parameters of biosonar are well known, a similar parallel-hierarchical organization has been documented in auditory cortex (Suga 1988). It is possible that analysis of the auditory scene in nonspecialist mammals is similarly organized. In this report, we quantitatively document how processing of frequency, amplitude modulation (AM), and frequency modulation by rat PAF neurons differ from processing by A1 neurons. Although there are some similarities between A1 and PAF, several clear functional differences exist between these 2 cortical areas.

Overview of Major Findings

Our study suggests that the rat PAF lacks a strict tonotopic map and appears to function as a higher level in the cortical hierarchy of auditory processing. The receptive field size of PAF neurons is considerably larger than A1 neurons. PAF neurons exhibit stronger responses to tones and broadband noise than A1 neurons. PAF neurons also have longer latencies and exhibit stronger adaptation and weaker synchronization to rapidly repeated sounds. Although A1 neurons can follow modulated stimuli up to ~10 Hz, a majority of PAF neurons exhibit a degraded ability to follow modulations faster than 5 Hz. The reduction of temporal and spectral resolution of PAF neurons is consistent with increased integration. Collectively, these results indicate that PAF neurons are clearly distinct from A1 neurons.

Cortical Representation of Frequency—A Comparison with Previous Studies

All well-studied mammalian species (including cat, primate, ferret, and rodents) have multiple topographically organized auditory fields (Horikawa and Suga 1991; Merzenich and Schreiner 1992; Thomas et al. 1993; Kowalski et al. 1995; Stiebler et al. 1997; Eggermont 1998; Rauschecker 1998b; Recanzone et al. 1999; Linden et al. 2003; Rutkowski et al. 2003; Bizley et al. 2005). The house mouse has at least 2 tonotopically organized fields and the gerbil at least 4 (Scheich et al. 1993; Stiebler et al. 1997; Linden et al. 2003). A study by Rutkowski et al. (2003) demonstrated a tonotopically organized AAF in the rat. AAF neurons in both rats and cats display phasic short latency responses to tone bursts similar to A1 neurons but exhibit significantly broader excitatory receptive fields (Rutkowski et al. 2003; Imaizumi et al. 2004). Another study has reported a nonprimary auditory area in rats located ventral to A1

with receptive fields that were characterized as multi-peaked and broadly tuned (Bao et al. 2003). Similarly, neurons in the nonprimary auditory fields in cats and the auditory belt regions in primates typically have large receptive fields (Heil and Irvine 1998a; Recanzone et al. 2000; Loftus and Sutter 2001). These results are comparable with the finding of reduced retinotopy in the higher order fields of the visual system (Van Essen et al. 1992). For example, visual cortex topography in the macaque motion processing area, V5, is generally degraded compared with V1 and V2.

In this study, we observed no systematic tonotopy across most animals in PAF even when we quantified topographic organization in every possible orientation. An earlier report of tonotopic organization by Doron et al. (2002) in rat PAF differed in several important ways. First, in our study high-density mapping of PAF was conducted in individual animals. As a result, our analysis included 2 and a half times as many PAF recording sites per animal. Second, and perhaps most importantly, Doron and colleagues reported topography of the frequency that evoked the greatest number of action potentials at a single intensity well above threshold. When we quantified the frequency that evokes a response at the lowest intensity (derived from the frequency-intensity tuning curve), no topographic organization was observed. Although these 2 frequencies are usually related, they are not always identical. Thus, it remains possible that frequency tuning for loud tones could be topographically organized, whereas frequency tuning for tones near threshold is not. It is also possible that the CF map exhibits a fractured tonotopy in PAF.

The observation that rat PAF neurons exhibited significantly broader frequency tuning compared with A1 neurons has been consistently reported (Sally and Kelly 1988; Kilgard and Merzenich 1999; Doron et al. 2002). Similar differences in frequency tuning have also been observed in these 2 fields in cats (Heil and Irvine 1998a; Loftus and Sutter 2001). Broader receptive fields outside of A1 have also been reported in AII and AAF of cats (Schreiner and Cynader 1984) and the AAF in rats (Rutkowski et al. 2003). Interestingly, anatomists have noted some neuroanatomical similarities between the rat TE2 area and the cat auditory field AII (Roger and Arnault 1989; Arnault and Roger 1990). Receptive field sizes tend to increase as sensory inputs progress up the cortical hierarchy regardless of modality.

Temporal Aspects of Cortical Processing in PAF and A1—Response Latency

Analysis of neural response latency has been useful in developing models of visual cortical function (Nowak et al. 1995; Bullier et al. 1996; Schmolesky et al. 1998). Studies of the sequence and duration of neural activation in distinct auditory cortical fields will likely be useful as we develop a more complete understanding of audition. Our goal was to compare auditory response latencies of A1 neurons with neurons in a nonprimary area that has received considerably less attention from experimentalists. The individual latency data presented in Figure 3 and the group data shown in Figure 6 establish that PAF neurons have longer times to first action potential, peak response, and termination of response compared with A1 neurons. Doron et al. (2002) also reported that the mean onset latency was typically longer and more variable in P than in A1. Similar latency differences between A1 and PAF have also been

observed in cats (Phillips and Orman 1984; Phillips et al. 1995; Loftus and Sutter 2001; Stecker et al. 2003).

Rutkowski et al. (2003) reported that AAF neurons in rats exhibit shorter response latencies than A1 neurons. A similar observation was reported in these fields for mice (Linden et al. 2003), cats (Eggermont 1998), and ferrets (Kowalski et al. 1995). Thus, it appears that AAF and A1 may combine to form the “core” of auditory cortex in rats (Doron et al. 2002; Rutkowski et al. 2003). Our latency results suggest that PAF is a higher field in the cortical hierarchy analogous to the “belt” regions described in primates (Rauschecker 1998b; Kaas and Hackett 2000).

Differences in average latency and topography of PAF and A1 may in part reflect differences in the connectivity underlying the auditory cortical areas. A precise correlation between anatomical and physiological extents of the auditory cortical fields in rats has yet to be established. Anatomic studies in the rat by Arnault and Roger (1990) determined that the core area TE1 receives most of its afferent projections from the ventral division of the medial geniculate. This projection is dense and topographically organized. In contrast, the TE2 region is preferentially connected to the ventrolateral sector of the dorsal division of the medial geniculate which appears to have no precise topographic arrangement. In light of prior neuroanatomical definitions, the distinctive differences in the functional response properties of the neurons recorded in this study, and the location of our recording sites, PAF appears to be located in TE2.

Representation of Temporal Modulations of Narrow and Broadband Sounds in PAF

Temporal modulations provide important information as to the identity of animal communication calls and many other naturally occurring sounds. These sounds often have complex temporal structures that contain both slowly and rapidly changing components. There is a progressive reduction in the maximum following rate from the auditory nerve to the cortex (Langner 1992; Eggermont 2001; Joris et al. 2004). In the cat, auditory cortical fields can be distinguished by their ability to respond to different rates of AM. More specifically, AAF and A1 can respond to AM tones at higher rates than AII, PAF, and VPAF (Schreiner and Urbas 1988). In the rat, a previous study using sinusoidal AMs reported no differences in the best rates of A1 and PAF neurons (Doron et al. 2002). In our study using repeated tone and noise bursts, we found that the limiting rate of PAF was significantly slower and response synchronization was reduced compared with A1. Most A1 neurons in rats respond well to trains of tones presented at rates below 10 Hz (Kilgard and Merzenich 1999). Here, we confirmed that the maximum following rate is the same for broadband stimuli (Fig. 10). In addition to anatomical differences in inputs, the lower maximum following rate of PAF neurons could indicate that there is more inhibition or synaptic depression in PAF compared with A1 (Buonomano and Merzenich 1998; Hefti and Smith 2000; Atzori et al. 2001)

The maximum following rate of rat PAF neurons was less than half that of A1, resembling the “low” temporal resolution fields described in anesthetized cats by Schreiner and Urbas (1988). Across studies, there is a wide variation in the reported best rates and maximum following rates, presumably due to variation in species, anesthetic state, and analytical methods used. Most

studies using an anesthetized preparation have found BMF vary between 1 and 40 Hz with a majority below 20 Hz using synchrony measures and 8 Hz using rate-based measures (Schreiner and Urbas 1988; Eggermont 1998; Joris et al. 2004). More recently, Wang and colleagues have shown that stimulus-following rates in response to click train stimuli in A1 were higher in awake marmosets than in anesthetized cats (Lu and Wang 2000; Lu et al. 2001), but to our knowledge, no direct comparisons within the same species have yet been made. In rodents, there are few if any studies documenting whether cortical fields outside the core areas respond with lower temporal fidelity in response to trains or pulses of discrete sounds.

Strength of Response to Tones and Noise in PAF

Earlier studies suggested that cortical neurons in nonprimary areas of primates are not effectively driven by tonal stimuli and prefer broadband sounds (Rauschecker et al. 1995; Rauschecker 1998a). In contrast, neurons in the PAF and dorsal zone in cats respond better to tones than to noise stimuli (Phillips et al. 1995; Stecker et al. 2003, in press). Our observation that PAF responds similarly to tones and noise differs from reports of nonprimary auditory cortex responses in both cats and monkeys. Rat PAF neurons respond more strongly to both tones and noise compared with A1 neurons. It is unclear whether the different preferences of nonprimary fields in rats, cats, and primates are due to genetic differences, experiential history, or the analytic method used to determine response strength to tones and noise.

Response to Frequency Modulations

Visual area MT contains neurons that are selective to direction and rate of visual motion (Maunsell and Van Essen 1983; Felleman and Kaas 1984). FM sweeps, which are in some ways analogous to moving light bars, have been used extensively to probe neurons at multiple levels of the auditory system (Kay 1982; Eggermont 2001; Nelken 2002). Although frequency modulation serves as an information bearing parameter in many natural sounds (Suga 1989), an auditory homolog of MT that is tuned to FM direction or rate independently of other acoustic parameters has not been identified. The broad excitatory receptive fields and longer latency of PAF neurons could support FM rate or direction tuning, however, we observed no selectivity for the direction of one octave FM sweeps. In general, the time course and the duration of activation of responses of PAF and A1 neurons to short FM sweeps were similar to the responses to short tones (Fig. 12). For long FM sweeps, additional action potentials were evoked in both fields. Although A1 neurons responded with more action potentials to a 160-ms sweep compared with a 40-ms sweep, PAF neurons did not. This is consistent with the longer duration of adaptation observed with repeated tones and noise (Fig. 10).

Our observation that the degree of PAF direction tuning can depend on sweep rate is consistent with previous studies. In cats, for example, more neurons preferring downward FM's have been documented in A1 compared with PAF neurons which prefer upward sweeps (Tian and Rauschecker 1998). A recent study by Tian and Rauschecker (2004) also described neurons in monkey auditory belt regions with DS that varied for FM's of different rates. Most studies of FM processing in auditory

cortex have used sweeps that span several octaves. Cat PAF neurons, for example, are direction selective to sweeps that span a wide frequency range (Tian and Rauschecker 1998; Heil and Irvine 1998b). Additional studies will be needed to determine whether rat PAF neurons exhibit direction or rate selectivity for wide FM sweeps.

Potential Roles of Rat PAF in Acoustic Processing

The long latencies and wide excitatory receptive fields exhibited by PAF neurons suggest that this field could sustain important integrative functions in processing the acoustic biotope. For the range of stimulus parameters used in this study, we observed no evidence of such a role. The question then arises, what role does rat PAF have in the processing of the auditory scene?

A recent cortical inactivation study has provided evidence that the cat PAF is required for spatial localization (Lomber and Malhotra 2003; Malhotra et al. 2004). Interestingly, cat PAF neurons share several response characteristics with rat PAF neurons, including broad receptive fields and long response latencies. Several studies have examined simple binaural interactions of rat A1 and PAF neurons (Kelly and Sally 1988; Kelly and Phillips 1991; Doron et al. 2002); however, there are no published reports of auditory spatial receptive fields in rat auditory cortex. Interest in examining the representation of auditory space in the PAF of rats has been increased by anatomical studies documenting that the TE2 region sends a projection to deep layers of the superior colliculus (Arnault and Roger 1990; Kimura et al. 2004), which has broad spatial tuning and a coarse topographic map of auditory space (Gaese and Johnen 2000).

The wider bandwidths of PAF neurons suggest that they may be involved in the extraction of spectral properties such as density and contrast. Sinusoidal ("ripple") and random spectrum stimuli have been used to explore the representation of broadband sounds in A1 (Schreiner and Calhoun 1994; Shamma et al. 1995; Calhoun and Schreiner 1998; Kilgard, Pandya, Vazquez, Rathbun et al. 2001; Barbour and Wang 2003). Parametric wideband stimuli such as these produce more complex cortical activation patterns than simple tones. It is possible that systematic physiological mapping of PAF using these and other complex sounds will reveal a topographic representation based on variations of spectral density, contrast, or bandwidth that could not be uncovered using tones or white noise.

Cortical Fields and Functional Specializations

The increasing numbers of studies aimed at identifying and quantitatively defining other auditory fields are important to accurately characterize the functional organization of auditory responsive regions of the neocortex. At least 4 auditory fields have now been physiologically identified in nearly every species studied ranging from rodents to primates. Our data on the spectral and temporal response profiles of rat PAF neurons, in conjunction with previous studies, show that the organization of the auditory cortex of the rat is comparable with the functional organization reported in many other species. Collectively, these studies lend support to the notion that acoustic signal processing occurs in both parallel and serial fashion throughout the auditory cortex and that cortical fields in rats can in large part be distinguished on physiological criteria. As in other modalities, a combined approach using

physiological mapping and neuroanatomical tracing studies will be crucial in delineating the modular and hierarchical organization of information processing in the auditory cortex (Luethke et al. 1988; Rouiller et al. 1991; Read et al. 2001; Lee et al. 2004). Additionally, the perceptual role that each of these functionally distinct fields plays in processing the acoustic biotope will need to be determined with behavioral studies.

Technical Considerations

Two methodological aspects of this study warrant brief mention. First, it should be noted that the functional data reported in this study were obtained from rats anesthetized with pentobarbital. Second, the action potential data collected in these experiments were derived using multiple unit recording technique.

Auditory cortex has long been known to be affected by anesthesia and these effects on cortical responses have been described in detail by other investigators (Zurita et al. 1994; Cheung et al. 2001; Gaese and Ostwald 2001). One must be cautious in generalizing the results from this study to neuronal activity in awake rats (Gaese and Ostwald 2003). In recordings obtained from awake marmosets, Wang et al. (2005) report that neurons from primary and lateral belt areas are capable of firing continuously and in a sustained manner when “preferred” stimuli are used. Although the basic organizational features of visual cortex, such as ocular dominance, retinotopy, and orientation tuning, are maintained under pentobarbital anesthesia (Stryker et al. 1987), it is possible that response properties in auditory cortex, especially nonprimary auditory cortex, are more sensitive to anesthetic state. Regardless, the reported comparisons in this study were with A1 responses recorded under identical conditions and in most cases in the same animals. A thorough comparison of neuronal responses under both anesthetized and unanesthetized conditions using the same stimuli should provide greater insight into the fundamental mechanisms underlying spectral and temporal processing in the PAF.

The multiple unit recording technique employed in this study offers several advantages. The primary advantage of multiunit recording technique is that it allows spatial distributions of neuronal response properties to be determined in fine topographic detail. An additional advantage is that responses recorded at each site reflect the summed activity integrated at that location and thus more accurately represents the mean activity at that site than would any given single unit. Given the large class of sounds used in this study, multiunit recordings were necessary to sample from as many cortical locations as possible. Because data derived from individual recordings sites represent the activity of several neurons, it is possible that individual neurons in each set were more narrowly tuned in frequency and sharper in latency than the summed activity. Whether or not individual neurons are as broadly tuned and temporally variable as the multiunit responses suggest, our results demonstrate that the functional organization of A1 and PAF differs significantly.

Conclusions on Functional Characterization of Rat PAF

Over the last 50 years, there has been a steady increase of anatomical and physiological information about the organization and connectivity of different sensory areas in the mammalian

cortex (Felleman and Van Essen 1991; Kaas and Collins 2001). Generally, the number of functionally identified cortical fields devoted to information processing of sensory features has increased as knowledge about the anatomy and physiology of different cortical regions has improved. This increase is in part due to the use of increasing complexity of stimulus features when probing sensory cortex using physiological mapping techniques. Examining several sensory features independently has been an extremely useful strategy in determining the functional specializations of cortical fields. This approach contributed to the development of specific models about different sensory processing streams (Ungerleider and Mishkin 1982; Rauschecker and Tian 2000), although the validity of these working models remains open to considerable debate and experimental investigation (Goodale and Milner 1992; Middlebrooks 2002).

Quantitative physiological data regarding the functional organization of nonprimary cortical fields and their response properties in the rat will be highly valuable given the use of this species for 1) behavioral studies using classical conditioning (Quirk et al. 1997), frequency discrimination (Syka et al. 1996), gap detection (Ison et al. 1991; Syka et al. 2002), sound localization (Kelly 1980), and modulation rate discrimination (Sakai et al. 1999); 2) cortical map and receptive-field plasticity studies in adults (Bakin and Weinberger 1996; Kisley and Gerstein 2001; Kilgard, Pandya, Vazquez, Gehi et al. 2001); 3) developmental plasticity studies (Metherate and Aramakis 1999; Chang and Merzenich 2003); and 4) in vivo and in vitro studies of synaptic coding and plasticity mechanisms (Atzori et al. 2001; Seki et al. 2003; Wehr and Zador 2003; Zhang et al. 2003). In addition, several experimental techniques that are readily available in this species provide a number of advantages when probing the molecular, cellular, and systems-level mechanisms of neural information processing.

In recent years, several studies of the auditory cortex have explored the cortical plasticity mechanisms and rules that may contribute to learning and memory (Edeline 2003; Suga and Ma 2003; Weinberger 2004). This research has focused primarily on A1 because of its relatively simple tonotopic organization. It is generally believed that early sensory areas encode only sensory properties and that nonprimary cortical areas are more directly involved in “higher” cognitive function (i.e., perception). Given the scarcity of plasticity studies in nonprimary auditory cortex, future studies will need to be directed toward evaluating the contributions of nonprimary areas for learning and memory to begin addressing questions about the relative plasticity in different levels of cortical processing (Woody et al. 1976; Kraus and Disterhoft 1982; Diamond and Weinberger 1984, 1986).

Notes

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