

# Listening Through Different Ears Alters Spatial Response Fields in Ferret Primary Auditory Cortex

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**Mrsic-Flogel, Thomas D., Andrew J. King, Rick L. Jenison, and Jan W. H. Schnupp.** Listening through different ears alters spatial response fields in ferret primary auditory cortex. *J Neurophysiol* 86: 1043–1046, 2001. The localization of sounds in space is based on spatial cues that arise from the acoustical properties of the head and external ears. Individual differences in localization cue values result from variability in the shape and dimensions of these structures. We have mapped spatial response fields of high-frequency neurons in ferret primary auditory cortex using virtual sound sources based either on the animal's own ears or on the ears of other subjects. For 73% of units, the response fields measured using the animals' own ears differed significantly in shape and/or position from those obtained using spatial cues from another ferret. The observed changes correlated with individual differences in the acoustics. These data are consistent with previous reports showing that humans localize less accurately when listening to virtual sounds from other individuals. Together these findings support the notion that neural mechanisms underlying auditory space perception are calibrated by experience to the properties of the individual.

## INTRODUCTION

The primary cues used to pinpoint the horizontal location of a sound source are differences in the time of arrival and level of sound between the two ears, whereas elevation judgments and front-back discrimination are based on the direction-dependent spectral filtering of sounds by the head and external ears. The directional transfer function (DTF) mathematically describes these acoustic transformations. Accurate measurements of acoustic cues for sound location make it possible to create a "virtual acoustic space" (VAS), where sounds presented over headphones appear to come from real sources out in space (Wightman and Kistler 1989).

Auditory localization cue values depend on the shape and dimensions of the head and ears and therefore vary between individuals (Middlebrooks 1999a; Middlebrooks and Green 1990; Shaw and Teranishi 1968). Consequently the correspondence between particular cue values and directions in space must be learned. Indeed, if VAS techniques are used to allow subjects to listen through someone else's ears, localization performance is impaired (Middlebrooks 1999b; Wenzel et al. 1993). In this study, we have identified a neural correlate for these behavioral results by using virtual sound sources to generate detailed spatial response fields of neurons in the

primary auditory cortex (A1) of the ferret. We chose to record from A1 because lesion studies in various species, including ferrets, have indicated that this area plays a central role in auditory localization (Jenkins and Merzenich 1984; Kavanagh and Kelly 1987).

## METHODS

### VAS implementation

At the start of each experiment, pinna DTFs were measured for each animal. During surgery and acoustical recording, the animals were anesthetized with alphaxalone/alphadolone acetate (Saffan, 2 ml/kg ip, supplementary doses given intravenously), and body temperature was maintained at 39°C. Custom probe microphones based on KE-4-211-2 capsules (Sennheiser, High Wycombe, UK) were surgically implanted in the wall of the ear canal as described in Carlile (1990). The head was fixed to a minimal head holder and positioned at the center of a vertical robotic hoop (radius, 65 cm) in an anechoic chamber. Golay codes (512 point) (Zhou et al. 1992) were used to measure DTFs, sampling the entire space at  $\sim 10^\circ$  intervals, except for a  $40^\circ$  wide region behind the animal and positions below  $-60^\circ$  elevation, which our hoop-mounted speaker could not reach. Signals were digitized at 80 kHz and anti-aliased at 30 kHz. Interaural time differences (ITDs) were extracted from the recorded impulse responses using cross-correlation after band-pass filtering (0.5–3.5 kHz). To implement the VAS, a bank of minimum-phase filters was created from the DTF amplitude spectra. VAS stimuli comprised 20-ms bursts of Gaussian noise filtered with the appropriate minimum-phase filters and delayed to generate appropriate ITDs. Stimuli were delivered using custom insert earphones (M. Ravicz; MIT, Boston, MA), which were calibrated prior to each experiment. Amplitude corrections, which equalized the headphone transfer functions, were incorporated in the VAS minimum phase filters.

### Electrophysiological recording

During electrophysiological recordings, anesthesia was maintained with pentobarbital sodium (Sagatal;  $2\text{--}3\text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ ) and paralysis was induced with gallamine triethiodide (Flaxedil;  $20\text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ ). The barbiturate dose was adjusted so that a stable and adequate level of anesthesia was maintained as assessed by measuring the electroencephalogram, electrocardiogram, and end-tidal  $\text{CO}_2$ . The left A1 was exposed, and single unit activity was recorded using tungsten-in-glass electrodes, TDT System II and BrainWare (Tucker-Davis Technologies, Gainesville, FL). We estimated the spatial response fields

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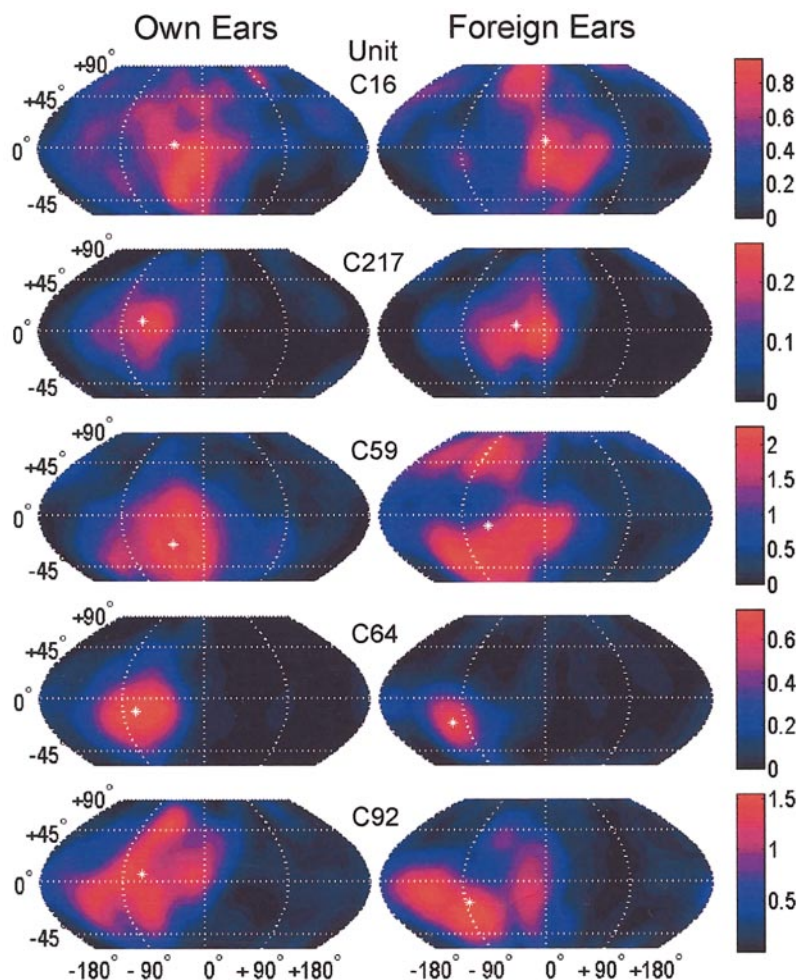


FIG. 1. Primary auditory cortex (A1) spatial response fields (SRFs) mapped using virtual acoustic space stimuli. Each row compares the SRFs of 1 unit measured with the animal's own auditory spatial cues (own ears) with those from another ferret (foreign ears). Broadband stimuli were presented from 224 virtual positions, covering  $360^\circ$  in azimuth and from  $-60^\circ$  to  $+90^\circ$  in elevation. Foreign-ear directional transfer functions (DTFs) produced changes in the structure of the response field that included shifts and fractures in azimuth and/or elevation. The centroids (\*) are spike-count-weighted centers of gravity calculated for all virtual sound directions. Scale bars indicate mean spike counts per stimulus presentation.

(SRFs) at sound levels of 15–45 dB above unit threshold by recording responses to VAS stimuli delivered from 224 different virtual source directions. Responses to five presentations from each virtual location were averaged with presentations from different locations randomly interleaved. Source direction was specified in spherical coordinates, and response fields were visualized using “equal area” geographical map projections. For each unit, we recorded SRFs with the animal's own ears and with at least one set of foreign-ear DTFs at the same sound level relative to unit threshold.

Experimental protocols were approved by the local ethical review committee and by the UK Home Office.

## RESULTS

We made 59 own-foreign ear comparisons from 46 units in three ferrets using both the animals' own DTFs and one or more sets of foreign DTFs. The best frequencies of these units ranged from 3 to 30 kHz. SRFs were predominantly broad and contralateral, and generally similar to those reported in cat A1 (Brugge et al. 1996).

In the majority of cases (73%), the SRF profiles changed significantly when tested with foreign rather than own-ear DTFs [ $P < 0.01$ , bootstrap test (Efron and Tibshiriani 1993); a parametric  $D^2$  test (Zelterman 1987) gave very similar results]. Switching from own to foreign ears resulted in shifts of the SRF or changes in SRF shape (see Fig. 1 for representative examples). Occasionally (5/46 cases), changing from own to foreign ears introduced splits (“fractures”) in the SRF profile

(e.g., Fig. 1, rows 3 and 6). Such fractures were not observed in the own-ear SRFs. But while the shape of the SRF profiles changed appreciably, SRF sizes remained very similar. Thus the regions of space where a response of  $\geq 50\%$  of maximum could be elicited covered an area of  $3.24 \pm 2.00$  (SD)  $\text{rad}^2$  in the own-ear SRFs, compared with  $3.05 \pm 2.20$   $\text{rad}^2$  for the foreign-ear SRFs.<sup>1</sup>

There was no difference in mean spike count between the responses obtained with different DTFs (own  $0.49 \pm 0.49$ , foreign  $0.49 \pm 0.69$  spikes; means  $\pm$  SD;  $P = 0.485$ ). As a measure of spatial preference, we calculated the position vector from the origin to the center of gravity (centroid) for each SRF. For this purpose, SRFs were modeled as spheres of unit radius. The neural response strength in a particular direction determined the density of the corresponding portion of the model sphere. The direction and length of the centroid gave a measure of the preferred direction and sharpness of tuning, respectively, of the SRF. Mean vectors calculated for own-ear SRFs were significantly longer, indicating sharper spatial tuning, than those for foreign-ear SRFs (own:  $0.26 \pm 0.12$ , foreign:  $0.23 \pm 0.12$  spikes, means  $\pm$  SD;  $P < 0.001$ , Wilcoxon signed test).

Differences in the centroid directions between own- and foreign-ear SRFs were distributed in a manner that depended on the DTFs used (Fig. 2). For example, substituting the DTF of *f0054*

<sup>1</sup> In comparison, an omnidirectional SRF, covering the entire unit sphere, would have an area of  $4\pi$  (12.57)  $\text{rad}^2$ .

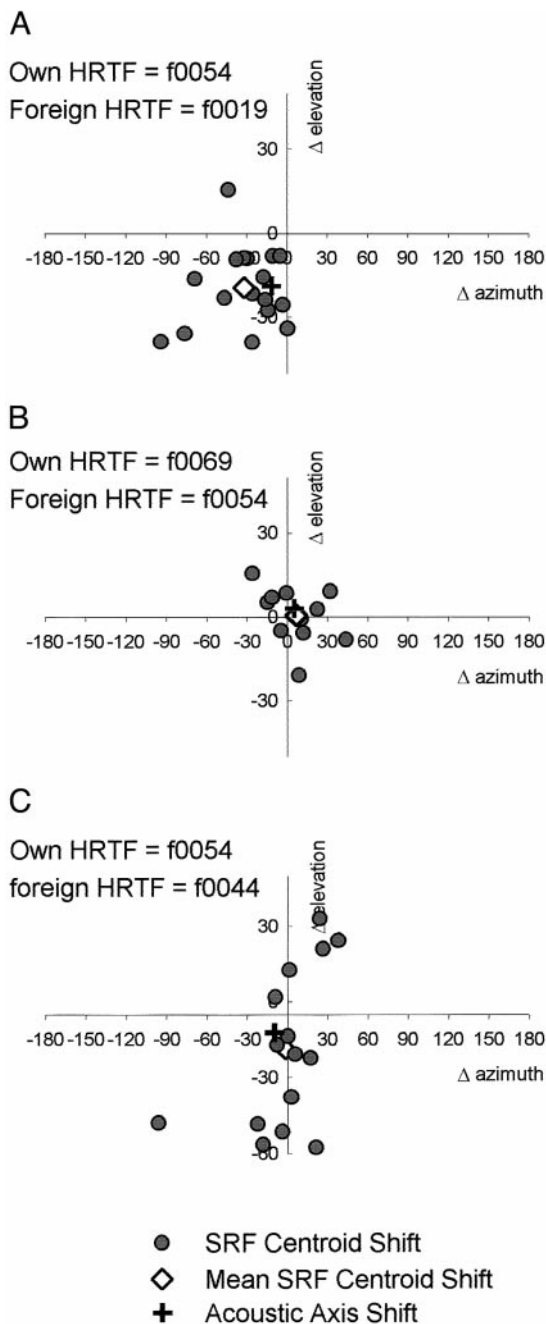


FIG. 2. These plots show the shift in the centroid of the spatial response fields when virtual acoustic space (VAS) stimuli were based on DTFs measured from another ferret rather than the animal's own ears. Each plot shows the distribution of centroid shifts for a different substitution of DTFs.

(own) with that of *f0019* (foreign) resulted predominantly in SRF centroid shifts toward the lower left quadrant (Fig. 2A), whereas substituting *f0069* (own) with *f0054* (foreign) DTFs produced shifts that scattered around the origin (Fig. 2B). A different distribution of centroid shifts was observed in *f0054* (same animal as in Fig. 2A) when DTFs from a juvenile male (*f0044*) were used to map SRFs. Here, the centroid shifts were distributed predominantly along the vertical plane (Fig. 2C).

In general, the changes in the SRFs could be partly accounted for by individual differences in the DTFs. Thus the SRF centroids shifted toward the "acoustic axis" of the con-

tralateral foreign ear (defined as the centroid of the DTF log energy function over a frequency band covering the best frequencies of the recorded units, see Fig. 2). Similar trends have also been observed in cat auditory nerve (Poon and Brugge 1993). Moreover, we found that the variance of the angular difference between own- and foreign-ear SRF centroids correlated with inter-subject spectral differences (Middlebrooks 1999a) in the corresponding DTFs. For example, the greatest range of SRF centroid shifts was present in the *f0054-f0044* pair (variance, 0.208 rad<sup>2</sup>; DTF spectral difference, 13.5 dB<sup>2</sup>), whereas the smallest shifts occurred in the *f0069-f0054* pair (variance, 0.035 rad<sup>2</sup>; DTF spectral difference, 10 dB<sup>2</sup>).

## DISCUSSION

We have examined the SRFs of A1 neurons using broadband VAS stimuli. This approach provides a faster and more detailed characterization of SRFs than is generally possible using free-field stimuli. Moreover by manipulating the signals presented at each ear, the spatial cues can be altered. Here we found that presentation of DTFs measured from other ferrets, rather than those representing the filter properties of the animal's own ears, produced significant changes in the structure of the SRFs of A1 neurons. We used fairly high sound levels at which both monaural and binaural cues are likely to contribute to the SRFs. Because our method of generating VAS stimuli with minimum phase filters produced minimal changes in mean sound level (<0.8 dB), when we switched from own to foreign ears, we can be confident that sound levels relative to unit threshold remained constant when assessing differences in SRFs. A recent study suggests that coding of space in cat area A2 may also be sensitive to DTF changes (Xu et al. 1999). Although the use of nonindividualized DTFs is appropriate for addressing certain questions (Brugge et al. 1996; Delgutte et al. 1999), these findings highlight the importance of generating VAS stimuli from an individual's own ears for investigating neural representations of space and their plasticity.

Our results are consistent with the reduced accuracy of sound localization exhibited by humans when listening through DTFs measured from someone else's ears (Middlebrooks 1999b; Wenzel et al. 1993). In both cases, changes in the apparent direction of the sound source were correlated with inter-subject differences in the DTFs. Indeed by frequency scaling the DTFs so that the principal spectral features more closely matched those of the subject's own ears, Middlebrooks (1999b) found that localization errors were reduced.

Together, these findings highlight the marked variations that exist between individuals in auditory localization cue values. Recent studies showing that both humans (Hofman et al. 1998) and ferrets (King et al. 2000) can learn to localize sounds accurately using abnormal spatial cues produced by physically modifying or occluding the external ear suggest that the neural representation of auditory space, either in A1 or at some higher level (Rauschecker and Tian 2000), should be equally plastic.

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