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Pursuing dynamic reorganization in auditory cortex using chronic, multichannel unit recordings in awake, behaving cats

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Abstract

We implanted microelectrode arrays bilaterally into auditory cortex of trained cats in order to assess dynamic cortical reorganization. Cats were trained to listen to a series of tone-pip pairs and respond to the pair that had different frequencies. Over several months of training, a gradual decrease (-4.2×10^{-4} Weber Fractions/training day) in the frequency discrimination threshold occurred ($p < 0.00001$). Neural recordings from a trained cat not performing the task were obtained for 5 days. Temporal and frequency response properties remained stable over this time. These techniques are useful for a variety of studies on learning-induced cortical plasticity. © 1999 Published by Elsevier Science B.V. All rights reserved.

Keywords: Auditory cortex; Plasticity; Behavior; Multichannel electrodes

1. Introduction

The frequency map in auditory cortex of the awake monkey exhibits learning-induced reorganization when a frequency discrimination task is performed [5]. Increases in cortical representation, tuning sharpness, and latency occur for stimulus frequencies relevant to the training task. Because the reorganization is documented by statistically comparing initial frequency response maps in control animals to end-point maps in trained animals, the cortical state at intermediate stages of reorganization could not be measured.

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Recent refinements in chronic microelectrodes and recording techniques now enable researchers to monitor simultaneous multiunit activity during a behavioral task. Using this technology, we investigated dynamic learning-induced cortical reorganization in the cat auditory cortex. These studies require that (1) trained cats with these implants improve at a frequency discrimination task and (2) recorded neural response properties exhibit relatively low variability during control experiments (e.g., passive stimulation). We have been able to demonstrate that cats can improve at a listening task, and neural recordings from an awake, inattentive cat can remain stable for at least 5 days.

2. Methods

2.1. Psychophysical training

Two adult cats with normal hearing were trained to press and hold down a lever that initiates a sequence of tone-pip pairs and release the lever only when a different frequency occurs for a food reward (Fig. 1). The task involved measuring the cat's ability to discriminate a frequency difference between a short tone at a fixed reference (target) frequency (chosen to be 5000 Hz) and an alternate frequency. The absolute frequency discrimination threshold (FDT) was defined as the change in frequency which corresponded to a 50% correct response, explicitly determined by a non-linear regression fit of the data using a two-variable sigmoid model [3]:

$$y = 50*(\tanh(mx + b) + 1).$$

2.2. Neural recording and auditory stimulation

Each cat received a bilateral implant of 33-channel, microelectrode arrays in auditory cortex; however, only a portion of these electrodes was suitable for

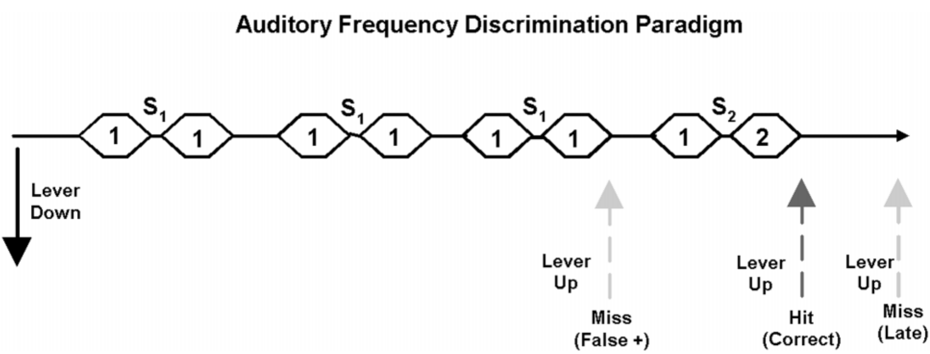


Fig. 1. Auditory frequency discrimination paradigm. Cats must discriminate between a target frequency (S_1) and alternate frequency (S_2) to receive a food reward.

prolonged day-to-day recording. (For details of data collection and recording procedures see [7].) Stimulus generation and behavioral feedback were administered using a computer-based sound system (Tucker-Davis Technologies Inc.). Data analysis was done primarily using software written in Mathematica and C. Frequency response areas (FRAs) were used to map unit responses to pure tone stimuli [6]. Each FRA consisted of a pseudorandom sequence of stimulus intensity and frequency (usually 20 frequencies equally spaced on a log scale from 1 to 35 kHz and 15 intensities from 30 to 100 dB SPL). Consecutive FRA sequences on a given day were separated by approximately 10 min. Unit spike counts were plotted for each stimulus frequency and intensity combination. Each auditory stimulus was delivered within an enclosed sound box in the free field using a single high-performance speaker placed directly above the cat's head.

Best frequencies (BFs) were determined by collapsing all sound levels for each presented frequency into a mean total response and normalizing to the total number of spikes of the FRA during the chosen interval around the stimulus. Any frequency that elicited a response higher than 3.1 standard deviations (99.9% confidence) above the mean background firing was designated as significant. Significant responses to each frequency were then fitted to a degree-4 polynomial for peak extraction. The peak of the polynomial fit represents the interpolated BF, and the peak width was determined at 75% of peak response to background firing. The degree driven (DD) for a unit was calculated by dividing the peak firing of the collapsed FRA by the mean background firing. Latency calculations for the sound stimulus was determined using an analogous fitting procedure with 3 ms bins.

3. Results

3.1. Performance improves with training

The auditory FDT progressively improved with training time (Fig. 2). Regular training days spanned four months. The mean FDT decreased ($p < 0.00001$) from 0.053 ± 0.008 WF (training days 1–20) to 0.043 ± 0.005 WF (days 21–49). The slope of the linear least-squares fit of the regular training data signifies gradual improvement of frequency discrimination at the target frequency. Although a second cat also demonstrated periods of an improved FDT, statistically significant conclusions regarding the trend of its FDT could not be established due to inconsistent daily performances marked by high false-positive rates.

3.2. Electrophysiology: Variability of neural responses to FRAs

During the first few days after operative preparation, onset responses for two multiunit clusters remained stable with passive listening to pure tones (Fig. 3A). The first two columns of Fig. 3A depict FRAs for these units taken at different intervals of time post-implant, denoted by the boxed number on the left (in days). FRAs on days 1,2 and 5a post-implant represent the response to the first FRA sequence recorded on

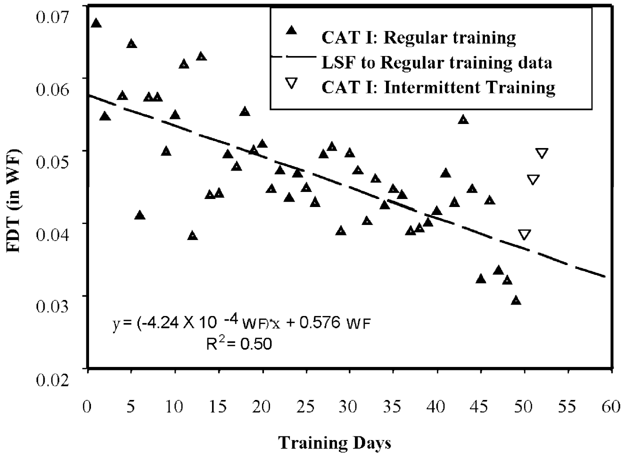
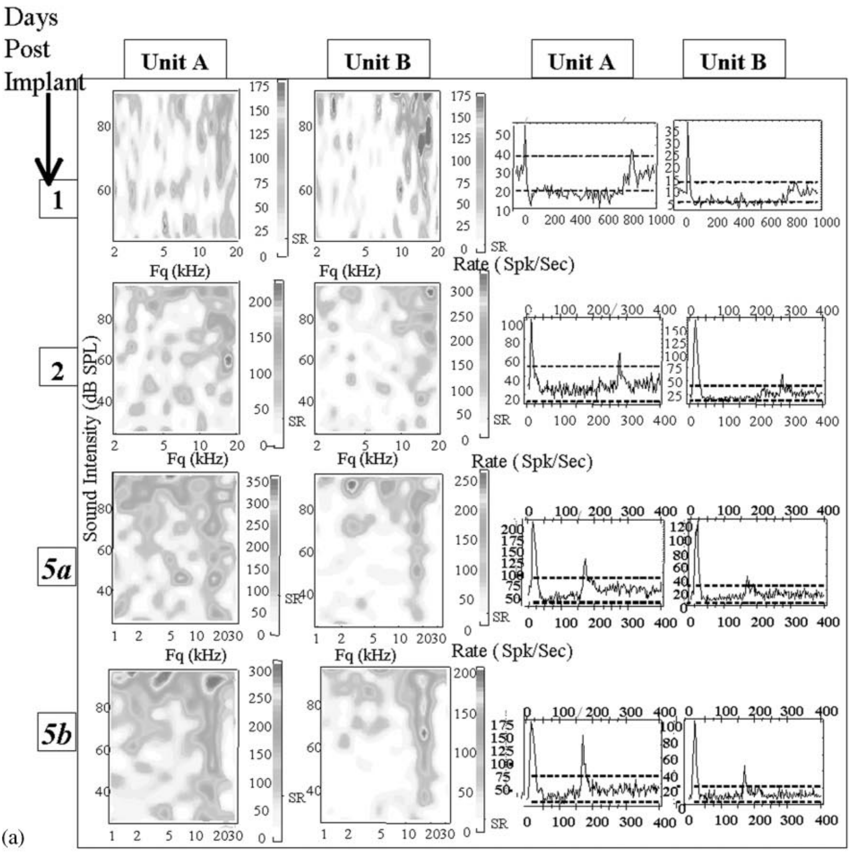


Fig. 2. Well-trained cat improved at listening task. FDT decreased ($p < 0.00001$) during the 4 months of regular training. Linear least-squares fit to data indicated a gradual decrease of the FDT of -4.2×10^{-4} WF/training day. Also, performance worsened with intermittent training ($p < 0.05$).

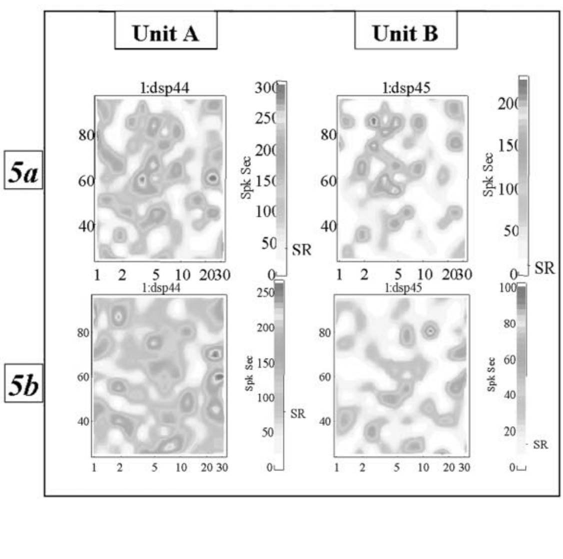
that day (note difference in scale). Day 5b represents the average of the 6th and 7th FRA sequence recorded on that day. The gray levels indicate average spike rate in spikes/s during a 40 ms window after the onset of the stimulus and plotted according to the frequency/intensity combination of the stimulus and interpolated. The last two columns of Fig. 3A show the PSTHs for the FRA sequence (for all frequency-intensity combinations). Intervals represent one full onset/offset period of the stimulus. Note a stable onset peak and a consistent offset response during the recording days. The stimulus content of the offset peak did not correlate well to the stimulus frequencies of the onset response; however, there seemed to be a consistent increased response to the offset of tones between 3 and 8 kHz at 60 dB SPL on day five (Fig. 3B). After the fifth day post-implant, daily monitoring of neural responses was no longer possible because the waveforms for these units could not be discriminated from the noise.

Table 1 shows that the specific response parameters for the two units (Unit A, Unit B) did not change appreciably during the daily recordings. Frequency parameters include BFs (kHz) with peak width (PkW) and degree driven at BF (DDf). Temporal parameters for the peristimulus time histograms (PSTH) of the FRA include latency (ms), peak width (PkW in ms), and degree driven at peak latency (DDt). Days are post-implant and "5_av" is an average of the seven valid FRAs taken on day five. The BFs (near 17 kHz) and temporal properties (within a day and across days) remain stable for these recordings.

Fig. 3. (A) Sample of FRAs (bin = 40 ms) and PSTHs (bin = 5 ms, abscissa = time (ms), ordinate = spikes/sec, tone onset at 0 ms, and tone offset at 750 ms on day 1, 250 ms on day 2, and 150 ms on day 5). For two multiunit clusters recorded simultaneously. Boxed number indicates days post-implant. Variability of BFs is relatively low, although units exhibit an increased stimulus response with increased recovery time. (B) FRAs of the offset peak for two separate recordings on day 5. There is an increase in frequency response to the offset of tones between 3 and 8 kHz near 60 dB SPL on day 5.


Days Post Implant
Unit A
Unit B
Unit A
Unit B
1
2
5a
5b
Sound Intensity (dB SPL)
Fq (kHz)
Rate (Spk/Sec)
SR

(a)


Unit A
Unit B
5a
5b
1:dsp44
1:dsp45
Spk Sec
SR

(b)

Table 1
Variability of frequency and temporal responses of the FRAs during 5 days post-implant. Best frequencies and latencies for each stay mostly within one standard deviation of the mean. "5_av" indicates the average responses for the 7 FRA sequences recorded on day 5

Unit A							Unit B						
Day	BF (kHz)	PkW (kHz)	DDF	Latency (ms)	PkW (ms)	DDt	Day	BF (kHz)	PkW (kHz)	DDf	Latency (ms)	PkW (ms)	DDt
1	16.6	3.3	2.0	14.2	17.8	2.2	1	16.4	3.3	6.2	18.7	19.2	5.4
2	16.2	3.4	3.2	12.9	19.4	3.2	2	14.4	4.8	4.5	15.7	11.8	5.5
5_1	17.4	6.4	2.5	14.7	12.3	3.3	5_1	17.0	6.3	6.8	16.6	9.0	6.8
5_2	17	7.5	2.4	13.7	13	3.0	5_2	16.2	6.8	5.6	16.5	8.5	7.8
5_3	16.2	6.8	2.8	14.4	12.5	4.3	5_3	17.0	6.1	9.7	15.9	8.4	12.7
5_4	16.6	5.7	2.6	14.1	12.9	3.2	5_4	16.2	6.3	7.8	15.7	11.7	8.5
5_5	16.2	6.8	2.9	14.3	9.5	3.2	5_5	16.6	11.3	8.3	16.2	9	9.2
5_6	16.6	5.7	2.9	14	12.4	2.8	5_6	16.6	5.8	8.3	18.3	19.6	6.1
5_7	16.6	7.2	2.6	15.1	10	3.1	5_7	16.6	6.9	7.9	17.5	20	8.2
5_av	16.6	6.6	2.7	14.3	11.8	3.3	5_av	16.3	7.1	7.8	16.7	12.3	8.5
	± 0.4	± 0.7	± 0.2	± 0.5	± 1.4	± 0.5		± 0.8	± 1.9	± 1.3	± 0.9	± 5.2	± 2.1

4. Discussion

Our findings demonstrate that a cat gradually improves at a frequency discrimination task as the FDT continues to decrease even after four months of training. The mean FDT of 0.04 WF over the second half of training parallels the performance of monkeys (also trained at 5 kHz). Monkeys, however, seem to learn the task and improve much more quickly [5]. Because cortical reorganization correlates directly with improvement of the animal's FDT, it is reasonable to hypothesize that the reorganization associated with a discrimination task takes longer in cats than in monkeys because of the different performance curves [5]. More cats need to be evaluated at the task to confirm these findings.

The neural recordings document that many response properties are stable for at least five days. The measured BF of each unit remains within one standard deviation of the mean (except for the FRAs recorded on day two for Unit B). Similar consistency in response latency is also observed. In contrast, a few response properties exhibit greater variability as demonstrated by broader PkWs at the BF for both units on day five compared to day one and two. Because these multiunit clusters are recorded simultaneously on neighboring electrodes (separated by $\sim 250\ \mu m$), similar response properties are expected due to a higher likelihood of cross correlation [1,2].

Despite the similarity of responses between the two units, functional differences are apparent. Unit B is consistently more strongly driven at the BF when compared to background firing and on average has a slightly longer latency (2+ ms) than Unit A, which suggests that each unit represents a slightly different space of the neural population. These differences are consistent with acute mapping experiments that describe response properties in isofrequency bands in AI of the cat (e.g. [4]). In addition to the onset response, a consistent offset peak occurred during the recording days. Because the offset peak does not directly correlate to the onset frequencies, this implies that different information about the stimuli may be encoded at different temporal intervals around the stimuli. This phenomenon further suggests that onset responses may not be the only metric of cortical reorganization.

With this work we provide evidence for stable response properties of chronic neural recordings during control experiments, and establish a basis for further investigation of cortical reorganization. Future experiments that produce implants with prolonged widespread unit activity should allow a more complete spatial representation of the cortical auditory field and, in the process, provide a more detailed description of learning-induced plasticity.

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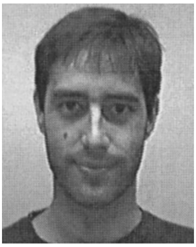

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