Behavioral training restores temporal processing in auditory cortex of long-deaf cats

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Vollmer M, Beitel RE. Behavioral training restores temporal processing in auditory cortex of long-deaf cats. J Neurophysiol 106: 2423–2436, 2011. First published August 17, 2011; doi:10.1152/jn.00565.2011.——Temporal auditory processing is poor in prelingually hearing-impaired patients fitted with cochlear prostheses as adults. In an animal model of prelingual long-term deafness, we investigated the effects of behavioral training on temporal processing in the adult primary auditory cortex (AI). Neuronal responses to pulse trains of increasing frequencies were recorded in three groups of neonatally deafened cats that received a cochlear prosthesis after >3 yr of deafness: 1) acutely implanted animals that received no electric stimulation before study, 2) animals that received chronic-passive stimulation for several weeks to months before study, and 3) animals that received chronic-passive stimulation and additional behavioral training (signal detection). A fourth group of normal adult cats that was deafened acutely and implanted served as controls. The neuronal temporal response parameters of interest included the stimulus rate that evoked the maximum number of phase-locked spikes [best repetition rate (BRR)], the stimulus rate that produced 50% of the spike count at BRR (cutoff rate), the peak-response latency, and the first spike latency and timing-jitter. All long-deaf animals demonstrated a severe reduction in spiral ganglion cell density (mean, <6% of normal). Long-term deafness resulted in a significantly reduced temporal following capacity and spike-timing precision of cortical neurons in all parameters tested. Neurons in deaf animals that received only chronic-passive stimulation showed a gain in BRR but otherwise were similar to deaf cats that received no stimulation. In contrast, training with behaviorally relevant stimulation significantly enhanced all temporal processing parameters to normal levels with the exception of minimum latencies. These results demonstrate the high efficacy of learning-based remodeling of fundamental temporal properties in cortical processing even in the adult, long-deaf auditory system, suggesting rehabilitative strategies for patients with long-term hearing loss.

long-term deafness; cochlear implant; perceptual learning; primary auditory cortex; neuroplasticity; temporal resolution

MEANINGFUL SOUNDS SUCH AS biologically relevant natural sounds and communication and vocalization sounds are largely recognized by their complex temporal modulation characteristics (Singh and Theunissen 2003; Shannon et al. 1995; Nagarajan et al. 2002; Wang et al. 1995). The auditory cortex is important for the perception of these time-varying features of sound (Joris et al. 2004). In humans, the temporal envelope is essential for the identification of phonemes, syllables, words, and sentences (Fu 2002; Rosen 1992). Moreover, it has been shown that the comprehension of speech is correlated with the capacity of auditory cortical responses to follow the frequency and the phase of the temporal envelope of the speech signal (Ahissar et al. 2001). Manipulations of normal acoustic experience during development result in deficits in the cortical temporal processing of rapidly successive stimuli that are associated with auditory and language impairments (Nagarajan et al. 1999; Temple et al. 2001; Wright et al. 1997). Importantly, prelingual hearing loss and long durations of deafness are associated with poor temporal processing (that is, poor rate and gap detection) and, consequently, deficient acquisition of auditory perceptual skills (Busby and Clark 1999; Busby et al. 1993; Eddington et al. 1978).

The majority of congenitally deaf subjects who receive a cochlear prosthesis early in life achieve speech perception comparable to that of postlingually deaf adults (Dowell et al. 2002). In contrast, congenitally and prelingually deaf cochlear implant (CI) users who are implanted late in life show particularly poor speech discrimination performance (Busby et al. 1991; Dawson et al. 1992; Ruben 1986). However, although the duration of deafness is inversely correlated with cortical activation and postimplant perceptual performance (Friedeland et al. 2003; Green et al. 2005), even individuals with long durations of deafness show some gradual improvement in speech discrimination performance with increasing auditory experience after implantation (Busby et al. 1991). This suggests that the amelioration of impaired speech comprehension is affected by the duration of deafness before implantation but is also influenced by auditory experience and learning-induced functional plasticity.

In hearing animals, it has been established that the primary auditory cortex (AI) is involved in learning-induced plasticity. Previous animal research has focused on learning-induced changes in acoustic frequency representation (e.g., Kisley and Gerstein 2001; Recanzone et al. 1993; Weinberger and Bakin 1998). However, recent studies in hearing animals have demonstrated that enrichment of the auditory environment (Engin et al. 2004) or behavioral training can markedly improve cortical temporal processing and response-timing precision. These improvements have been observed not only in the developing auditory system (Zhou and Merzenich 2009) but also in the adult auditory system (Bao et al. 2004; Beitel et al. 2003; Engineer et al. 2008; Leon et al. 2008; Schnupp et al. 2006). In deaf animals, research has emphasized changes in the spatial representation of electric cochlear stimulation (Fallon et al. 2009; Raggio and Schreiner 1999). A recent study (Beitel et al. 2011) has documented that behavioral training with
electric intracochlear stimulation enhanced AI neuronal temporal processing in profoundly deaf juvenile cats with substantial preservation of the peripheral innervation density.

We predicted that cortical temporal processing would be severely diminished in deaf adult animals deprived of all acoustic and electric hearing experience starting very early in life and continuing over long periods of time. We also hypothesized that in such long-deaf animals meaningful auditory experience and perceptual learning would be required for effective temporal plasticity in cortical field AI and for the amelioration and recovery from auditory deprivation and deafness. However, because of the prolonged deafness, the consequent severe loss of spiral ganglion cells (SGCs) and both functional and morphological changes in the central auditory system, we expected possible plastic effects to be smaller than those observed in deaf juvenile cats.

To test these hypotheses, neonatally deafened cats received a cochlear prosthesis after >3 yr of deafness and were assigned to one of three groups, defined by electric hearing experience: 1) animals that received no electric stimulation until the final electrophysiological experiment, 2) animals that received chronic-passive stimulation for several weeks to months before study, and 3) animals that received chronic-passive stimulation and additional behavioral training (signal detection of temporally modulated intracochlear electric stimulation). Previously normal hearing, acutely deafened, and implanted adult cats served as the control group. Temporal response properties of AI neurons were compared across groups to evaluate stimulus or task-specific differences in temporal processing among the experimental groups.

The objectives of the present study are threefold. First, we document the profound effects of neonatally induced long-term deafness (>3 yr) on temporal coding characteristics of AI neurons (repetition rate following, response latencies, and variability in spike timing). The second goal is to determine whether plastic changes in cortical temporal processing occur in the long-deaf auditory system and to investigate whether auditory experience can ameliorate or even reverse the effects of long-term auditory deprivation in AI neurons. The third goal is to investigate whether the criteria for temporal processing will be differentially affected by meaninglessness of chronic-passive electric stimulation of the cochlea vs. perceptual learning based on training with temporally structured signals. The results are compared with results obtained in short-term deaf juvenile cats that underwent similar passive and behaviorally relevant chronic stimulation regimes (Beitel et al. 2011).

METHODS

Some of the experimental procedures have been described in detail in previous reports (e.g., Beitel et al. 2000a, 2011; Schreiner and Raggio 1996; Snyder et al. 1995; Vollmer et al. 2001, 2007) and will be repeated here in an abbreviated form. All surgical and experimental procedures were approved by the Institutional Animal Care and Use Committee of the University of California, San Francisco and conformed to the guidelines of the National Institutes of Health for the care and use of laboratory animals.

Deafening procedures. The deafness, chronic stimulation, and behavioral training histories of the four groups of cats included in the present study are summarized in Table 1. Six cats were deafened as newborns by the systemic administration of neomycin sulfate (60–70 mg/kg im sid) beginning the day after birth and continuing for 16–25 days (e.g., Leake et al. 1987, 1991). Neomycin injections were terminated when profound hearing loss (>105 dB) was confirmed by the absence of auditory brainstem responses to clicks (0.2 ms/phase, 20 pulses per second (pps)). None of the animals demonstrated any residual hearing at the time of study. The animals were studied as adults after prolonged periods of deafness of >3 yr (range: 38–86 mo) and are referred to as long-deaf animals. The animals were divided into three experimental groups. Two animals did not receive any chronic electric cochlear stimulation. They were implanted with unilateral CIs as adults ≥1 wk before the electrophysiological experiment to allow thresholds to stabilize and were studied acutely [long-deaf unstimulated animals (LDU group)]. Two cats were implanted unilaterally and then received several weeks to months of chronic-passive electric stimulation as adults before study [long-deaf stimulated animals without behavioral training (LDS(−) group)]. Electric stimulation of the auditory nerve in these animals was initiated at an average age of 6.5 yr. The remaining two long-deaf animals were chronically stimulated starting at an average age of 4.9 yr and received additional behavioral training [LDS(+) group]. Two normal hearing adult cats were acutely deafened by coadministration of kanamycin and ethacrynic or aminooxyacetic acids (Leake et al. 1987; Xu et al. 1993) and were implanted 2 wk before study (control group). Spiral ganglion survival in the control group is assumed to be normal following previous observations (Leake and Hradek 1987).

Electrode design and implant surgery. Before all surgical procedures, the animals were sedated (ketamine: 22–33 mg/kg; acepromazine maleate: 0.1 mg/kg), and anesthesia was induced by pentobarbital

Table 1. Deafness and stimulation histories for the control and long-deafened experimental groups

<table>
<thead>
<tr>
<th>Group/Cat</th>
<th>Deafness</th>
<th>Chronic Passive Stimulation</th>
<th>Behavioral Training</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age at Deafness</td>
<td>Duration of Deafness, mo</td>
<td>Age at Initial Stimulation, mo</td>
</tr>
<tr>
<td>Control</td>
<td>CH617</td>
<td>Adult 0.5</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>CH958</td>
<td>Adult 0.5</td>
<td>NA</td>
</tr>
<tr>
<td>LDU</td>
<td>K51</td>
<td>Neonate 78</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>K73</td>
<td>Neonate 38</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>CD393</td>
<td>Neonate 79</td>
<td>73</td>
</tr>
<tr>
<td></td>
<td>K56</td>
<td>Neonate 86</td>
<td>84</td>
</tr>
<tr>
<td>LDU</td>
<td>CH618</td>
<td>Neonate 60</td>
<td>52</td>
</tr>
<tr>
<td></td>
<td>CH539</td>
<td>Neonate 69</td>
<td>65</td>
</tr>
</tbody>
</table>

NA, not applicable; SP, speech processor; pps, pulses per second. *Cat CH539 received limited stimulation with SP for the first 12 days.

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sodium (7–10 mg/kg) delivered via an intravenous catheter. An areflexic level of anesthesia was maintained during surgery by intravenous infusion of pentobarbital sodium in Ringer solution.

Cochlear implant electrodes consisted of custom-made Teflon coated platinum-iridium (90:10%) ball electrodes embedded in a silicone rubber carrier (Rebscher et al. 2000). The intracochlear electrode arrays had four bipolar contacts (250–290 μm diameter) arranged as two offset-radial pairs and were implanted into the left scala tympani.

**Chronic-passive stimulation [LDS(−) and LDS(+) groups].** In the LDS(−) and LDS(+) cats, chronic-passive electric stimulation was applied for ~4 h/day, 5 days/wk for a mean duration of 20 ± 12 (SD) wk. All of these animals were stimulated in bipolar mode using the apical electrode pair 1,2 (contact separation of 1 mm). Stimulating contacts were located on average at 49% (electrode 1) and 45% (electrode 2) of basilar membrane distance from the cochlear base, corresponding to frequencies of ~5.0–6.3 kHz (Greenwood 1974, 1990; Liberman 1982). Due to lead failure, subjects CD393 and CH539 were stimulated with electrode pairs 2,3 and 1,4, respectively, during the final weeks of stimulation.

Chronic electric stimulation was delivered either by an analog speech processor that transduced ambient environmental sounds into electric signals or by computer-generated amplitude-modulated pulse trains. The frequency spectrum of the analog speech processor was band-pass filtered from 250 Hz to 3 kHz with a roll-off at the shoulder frequencies of 6 dB/octave. The processor output was logarithmically amplitude-compressed to a dynamic range of 6 dB. The maximum peak-to-peak output was set to 6 dB above the electrically evoked auditory brainstem response (EABR; Moore et al. 2002) for each individual subject. Temporally modulated trains of electric charge-balanced biphasic square-wave current pulses (0.2 ms/phase) were generated by a computer (National Instruments, LabView) and were delivered through an attenuator (HP 350B) to an optically isolated constant current stimulator. Electric pulse trains were delivered continuously at a ~300-pps carrier rate and sinusoidally amplitude-modulated (SAM) at a frequency of 30 Hz with a modulation depth of 100% (300/30 SAM). The peak intensity of the SAM signal was set to 2 dB above the animal’s individual EABR threshold. This intensity was also above behavioral detection thresholds and minimum neural response thresholds in AI (Beitel et al. 2000a). The choice of these stimuli was based on previous studies (Snyder et al. 1995; Vollmer et al. 1999, 2005) showing that chronic electric stimulation of the developing and the long-deaf adult auditory system using these signals resulted in a significant increase in neuronal temporal processing in the central nucleus of the inferior colliculus (ICC). EABR thresholds and electrode impedances were measured at regular intervals to assess the stability and reliability of the cochlear implants and to adjust stimulation intensity if thresholds shifted.

**Psychophysical procedures [LDS(+) group].** Signal detection training was based on a conditioned avoidance paradigm as illustrated in Fig. 1A (Beitel et al. 2000a, 2011; Vollmer et al. 2001). A cat was trained to lick a metal spoon to obtain a preferred food reward (meat puree). A computer monitored contact with the spoon (sampling rate = 50 Hz), and the puree was delivered at a constant rate during Safe trials (60–70% of trials) when the cat was licking the spoon. On Safe trials, electric signals (National Instruments, LabView) were never delivered to the cochlea. On Warning trials (30–40% of trials), an electric warning signal or conditioned stimulus (CS) was presented, and the cat was required to interrupt licking to avoid a mild electrocutaneous shock or unconditioned stimulus (US). A light located above the spoon was turned on and off simultaneously with the US (140–210 ms duration) to provide visual feedback for successful avoidance. After several suprathreshold Warning trials, a cat typically began to avoid the US.

Once performance stabilized from session to session, threshold testing was initiated using the method of constant stimuli. The CS was presented during a session within a range of stimulus levels (5–10 dB, 1-dB steps) that bracketed the estimated threshold. Warning trials occurred randomly during a session, with the restriction that they could not occur successively. Perceptual learning was documented by an animal’s ability to detect temporally modulated signals at successively lower amplitudes over training sessions. Detection typically improved during training, confirming perceptual learning (Beitel et al. 2011). Threshold estimation continued until threshold performance from session to session varied within 2 dB for a particular stimulus condition. Psychophysical data from three sessions at the end of testing were corrected for false alarm rate and were pooled to derive mean 50% detection thresholds for each cat. Figure 1B shows final, stable mean thresholds for three trained long-deaf animals.

**Electrophysiological recording procedures.** At the end of chronic-passive and behavioral stimulation periods, the animals were studied electrophysiologically in acute, terminal experiments. Under the surgical protocol described above, the anesthetized animal’s head was stabilized in a standard head holder. The temporal muscle was retracted, a craniotomy was performed to expose the auditory cortex,
and the dura was reflected. A video image of the cortex was obtained and used to plot the locations of the electrode penetration sites that were made at closely spaced intervals (~0.5 mm) across AI as judged by sulcal boundaries. Responses of single neurons and multineuronal clusters were recorded using a differential recording technique with two impedance-matched parylene-coated tungsten microelectrodes (Microprobe; impedances ~1–1.2 MΩ at 1 kHz). The return electrode was placed at the surface of the cortex, and the recording electrode was advanced into layers IIIb or IV of the cortex at intracortical depths of ~600 to 1100 μm. Spiking activity was amplified, bandpass filtered, and monitored on an oscilloscope and an audio monitor. Response thresholds to biphasic pulses delivered at intensities just sufficient to activate the neurons were determined using audiovisual criteria. Spiking activity was isolated from background noise using a window discriminator (BAK DIS-1), and the number and arrival time of spikes per stimulus presentation were recorded and stored digitally.

**Parametric response measurements.** To assess the temporal processing capabilities of cortical neurons, trains of charge-balanced biphasic current pulses (0.2 ms/phase) at increasing pulse rates (2 to ~40 pps in 2 pps increments; 15–20 repetitions) were presented at electric current levels of ~2–8 dB above the audiovisually determined neuronal thresholds. Pulses were generated by computer (TMS32010) at a sampling rate of 60 kHz and delivered through an audio attenuator to an optically isolated constant current stimulator. The system was calibrated to a common reference level (0 dB = 1 μA peak-peak) before each recording session. Pulse trains were 500 ms in duration and were followed by a silent 1-s intertrial interval. With the exception of the lowest pulse rate (2 pps), responses to the first pulse in each repetition were excluded from the analysis to avoid stimulus onset effect. Responses to the varying rates were displayed in poststimulus time histograms (PSTHs; Fig. 2, A and B) and were analyzed quantitatively to obtain the mean onset time of the first spikes (mean minimum latency) across all repetitions at a pulse rate of 2 pps (see Fig. 6, A and B). The SD of the first spike times over all repetitions also was determined to provide an estimate of the temporal precision or jitter of the response onset (Ter-Mikaelian et al. 2007).

From the PSTHs, period histograms were derived excluding stimulus artifacts, and the vector strength (VS) and the number of phase-locked spikes (sp = total number of spikes * VS; P of VS < 0.01, Raleigh-test; Mardia 1972) evoked by each repetition rate at each recording site in each cat were determined (Fig. 2, C and D).

![Fig. 2. Poststimulus time histograms (PSTHs; A and B) and period histograms (C and D) of neuronal responses to pulse trains of increasing frequencies. A and C: examples for a long-deaf unstimulated (LDU) animal (K51). B and D: examples for a long-deaf stimulated (LDS) animal that received additional behavioral training (CH539). Best repetition rates (BRR) and cutoff rates are identified in A–D. Vertical lines in A and B mark onset of the stimulus pulses. Period histograms in C and D are derived from the PSTHs in A and B. In C and D, vector strength (VS) and the number of phase-locked spikes (sp = total number of spikes * VS) are shown at right of each histogram. All responses are significantly phase locked (P < 0.01). Arrows in C and D indicate peak latencies (i.e., modal latencies of the period histograms) determined at 2 pulses per second (pps). Bin width = 1 ms.](http://jn.physiology.org/doi/10.1152/jn.00916.2010)
In addition, the peak or modal latency was determined from the period histogram at the lowest stimulus rate (2 pps; Fig. 2, C and D).

Repetition rate transfer functions (RRTFs) were constructed by plotting the number of phase-locked spikes for the different stimulus repetition rates (Fig. 3). For each recording site (N = 168), two phase-locked response variables were determined: the pulse rate that evoked the largest number of phase-locked spikes (best repetition rate [BRR]) and the stimulus rate at which the number of phase-locked spikes fell to just below 50% of the number at BRR (cutoff rate). Figure 3 illustrates examples of RRTFs constructed for single recording locations in a LDU animal (Fig. 3A) and a LDS(+) animal (Fig. 3B). BRRs and cutoff rates are identified for each RRTF.

Cochlear histology. After completion of the electrophysiological experiment, cochlear and transcerebral perfusions were performed with histological fixative (2.5% paraformaldehyde and 1.5% glutaraldehyde in 0.1 M phosphate buffer), and the temporal bones and brains of all long-deaf animals were removed for histological examination using previously described methods (Leake et al. 1999). Briefly, cochleae were dissected, embedded in epoxy resin, and reconstructed in surface preparations to measure the basilar membrane. Radial semithin sections (1–2 μm) were cut at 50 μm intervals and stained with toluidin-blue. With the use of light-microscopy, SGC density was determined for each animal using a point-counting method. Earlier studies in normal hearing animals using this method provided normative data for the cat spiral ganglion (Leake and Hradek 1988). These data served as a control reference in the present study and allowed the SGC density of the long-deaf cats to be expressed as percentage of normal.

Statistical analyses. For normally distributed data, the descriptive statistics reported are the mean ± SD. If the data were not normally distributed, the median and the quartile deviation (Q) are reported. For normally distributed data, the descriptive statistics reported are the mean ± SD. If the data were not normally distributed, the median and the quartile deviation (Q) are reported. For normally distributed data, the descriptive statistics reported are the mean ± SD. If the data were not normally distributed, the median and the quartile deviation (Q) are reported. For normally distributed data, the descriptive statistics reported are the mean ± SD. If the data were not normally distributed, the median and the quartile deviation (Q) are reported.

RESULTS

SGC survival. All SGC densities reported in this study refer to the implanted left cochlea of each animal. The long-deaf animals demonstrate a severe decrease in SGC densities compared with normal (Table 1; Vollmer et al. 2005, 2007). The LDU group has the shortest duration of deafness (mean 58 mo) and demonstrates a mean SGC survival of 11.6% of normal. The deafness durations in the LDS(−) and the LDS(+) groups averaged 83 and 65 mo, respectively. These two groups demonstrate reductions in mean SGC densities to 4.3 and 2% of normal, respectively.

Behavioral training. Mean detection thresholds for each cat based on results from three threshold estimation sessions at the end of training are presented in Fig. 1B. The psychophysical threshold for detection of 300/30 SAM in cat CH618 is 47.3 ± 0.3 (SD) dB. In cat CH539, the detection threshold for a temporally modulated signal (30 pps) is 46.5 ± 1.3 (SD) dB. In a third long-deaf animal (K55) reported in a previous study (Vollmer et al. 2001), psychophysical detection threshold for 300/30 SAM is 37.5 ± 0.5 (SD) dB. As reported for profoundly deaf juvenile cats (Beitel et al. 2011), long-deaf cats studied behaviorally also demonstrate reliable psychophysical performance, perceptual learning over training sessions, and stable detection thresholds for electric stimuli in the final stage of training.

Temporal processing: BRR and cutoff rate. The primary objective of this study was to determine temporal coding characteristics of AI neurons to repetitive electric stimuli presented to the cochlea and to correlate the results with deafness duration and differences in auditory experience. Responses of 168 single neurons or multineuron clusters to contralateral cochlear stimulation were recorded in the right AI of 8 animals. PSTHs and period histograms were quantitatively analyzed to compare a number of parameters of neuronal temporal coding. Figure 2, A and B, shows examples of PSTHs for two neurons in response to increasing pulse rates for a LDU cat (Fig. 2A) and a LDS(+) cat (Fig. 2B). The period histograms in Fig. 2, C and D, are derived from the PSTHs in Fig.
and B, and display the varying degrees of phase locking (VS) and numbers of phase-locked spikes (sp) for the different electric pulse rates. The phase-locked spike rates are plotted as a function of pulse rates to construct RRTFs (Fig. 3, A and B). For all groups of animals, the majority of RRTFs (>50%) had band-pass functions with distinct maxima (BRRs) and a reduction of the number of phase-locked spikes on the high and low rate side of the BRR to ≤50% of the spike rate at BRR. However, LDU animals had a significantly higher proportion of low-pass RRTFs (47.1%) compared with the controls, LDS(−) and LDS(+) animals (5.6, 21, and 19.5%, respectively; χ², P < 0.001). In the illustrated examples, the RRTF of the LDS(+) animal (Fig. 3B) is shifted towards higher pulse rates resulting in a higher BRR and a higher cutoff rate (12 and 18 pps, respectively) compared with the LDU animal (6 and 10 pps, respectively; Fig. 3A).

Figure 3C shows mean phase-locked spike rate in the four groups of cats over the range of electric pulse rates (4 to 22 pps) that produced the most dynamic spike rate responses. In groups LDS(+), control, LDS(−), and LDU, peak phase-locked spike rates occur at successively lower pulse rates (20, 14, 12, and 6 pps, respectively). Peak phase-locked spike rate is highest in the behaviorally trained LDS(+) animals (27 spikes/s), lowest in the LDU animals (8 spikes/s), and intermediate in the control and LDS(−) groups (15 spikes/s and 10 spikes/s pps, respectively). The four functions clearly show the effects of different kinds of hearing experience on temporal modulation of neuronal responses in AI.

Figure 3C, inset, illustrates the proportion of neuronal recording sites (units) that contribute to mean phase-locked spike rate as a function of electric stimulus pulse rate. As pulse rate increases, the proportions of contributing units in the LDU, LDS(−), and LDS(+) groups decline. In the LDU group, the decline in the contributing number of units starts at 10 pps, and at rates ≥20 pps < 20% of the units contribute to the mean number of phase-locked spikes. The decline in the LDS(−) group starts at 12 pps. Both LDU and LDS(−) groups show similarly steep slopes, consistent with the impoverished hearing experience in these groups. In group LDS(+), the decline occurs after 18 pps with a shallower slope, and in the control group virtually no decline occurs up to 30 pps.

Figure 4, A and D, shows the quantitative distributions of BRRs and cutoff rates, respectively, for the four groups of animals. The BRRs of 168 unit responses to pulse trains of increasing frequencies are included in the present study. The number of unit cutoff rates included in the analysis is

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**Fig. 4.** Psychophysical training enhances cortical rate following. A and D: quantitative distribution of BRRs (A) and cutoff rates (D) for the 4 groups of animals. Bin size = 4 pps. Numbers in brackets indicate number of recorded units for each group of animals. B and E: cumulative probability of BRRs (B) and cutoff rates (E) for the 4 groups of animals (color-coded). Dashed horizontal line indicates that 90% of the units have a BRR (B) or cutoff rate (E) equal to or smaller than the corresponding value on the abscissa. C and F: statistical comparisons of median BRRs (C) and cutoff rates (F). Graphs plot the median, 10th, 25th, 75th, and 90th percentiles as vertical boxes with error bars. Dots indicate values above the 90th and below the 10th percentile. Kruskal-Wallis one-way ANOVA on ranks, P < 0.001; Dunn pairwise multiple comparison, *P < 0.05, **P < 0.01.
slightly lower (total of 140 units) because the recordings were not always continued until the criteria for cutoff rates were met (number of phase-locked spikes equal or just ≤50% of BRR) or the units had high-pass RRTFs for which the number of phase-locked spikes on the high cutoff side of BRR did not reach ≥50% of BRR. For control, LDS(−) and LDS(+) animals, the peak of the BRR distribution is located at 14 pps (Fig. 4A). In contrast, for LDU animals the distribution of BRRs is shifted towards lower pulse rates and peaks at 6 pps, reflecting a deterioration of the temporal following capacity in animals totally deprived of auditory input. The distribution of BRRs for LDS(+) animals covers the broadest range of frequencies and extends to higher frequencies than those for the other three groups of animals.

The peak of the distribution of cutoff rates (Fig. 4D) is identical for control and LDS(+) animals (22 pps), whereas the peak of the distribution of cutoff rates for LDU animals is ~1 octave lower (10 pps). The peak of the distribution for the LDS(−) animals is located at an intermediate cutoff rate value (18 pps). The overall distributions of cutoff rates in the control and LDS(+) animals are shifted towards higher frequencies compared with the LDU and LDS(−) animals.

Figure 4B shows the cumulative probabilities for BRRs in the four groups of cats. Across all groups of animals, the function for group LDU has the steepest slope and is shifted towards the lowest BRRs. Less than 10% of all neurons (i.e., values above dashed line) have BRRs >8 pps. This indicates a clear deterioration of cortical temporal following capacity due to auditory deprivation. The BRR functions for LDS(−) and control animals have similar slopes. However, the function for LDS(−) animals is shifted towards lower frequencies than that for control animals. In the LDS(−) animals, only ~10% of the neurons have BRRs >12 pps. In contrast, in the control animals ~10% of the neurons have BRRs of 19 pps or higher. This indicates that passive electrical stimulation in LDS(−) animals improves temporal following capacity compared with LDU animals, but the improvement does not reach normal levels. The curve for LDS(+) animals has the shallowest slope and is shifted towards the highest BRRs, thus, reflecting the clear distribution towards higher frequencies shown in Fig. 4A. Around 10% of the neurons in LDS(+) animals have BRRs of 29 pps and higher. This indicates that behavioral training completely recovered temporal following capacity and even improved it to levels above prior normal hearing control animals.

The cumulative probabilities for cutoff rates in Fig. 4E show trends that are similar to those for BRRs (Fig. 4B) with the exception that the curves for control and LDS(+) animals have similar shallow slopes and are shifted toward similar, higher frequencies. Around 10% of the neurons for both control and LDS(+) animals have cutoff rates of 35 pps and higher. In contrast, in the LDS(−) group, ~10% of the neurons have cutoff rates of 20 pps and higher, and in the LDU group, ~10% of the neurons have cutoff rates of 16 pps and higher.

As mentioned above, the number of neurons for which cutoff rates were determined was somewhat lower than that for BRRs, because the criteria for cutoff rates could not be met for a number of recordings. That is, the recordings were not continued to higher pulse rates required to determine the cutoff rate. As a result, the distribution of cutoff rates might not reflect the full extension of cutoff rates on the high frequency side and may slightly underestimate the actual values. The difference between the number of BRRs and cutoff rates is particularly large for LDS(+) animals. While the distribution of BRRs for LDS(+) animals is extended to higher frequencies than that for control animals (Fig. 4, A and B), the failure to consistently present higher frequency pulse rates could have reduced the distribution of cutoff rates in the LDS(+) group to frequency values that are only slightly higher than those recorded in control animals (Fig. 4E).

Figure 4, C and F, summarize the statistical comparisons of BRRs and cutoff rates, respectively, for the four groups of animals (Kruskal-Wallis one-way ANOVA on ranks, P < 0.001; Dunn pairwise multiple comparison). Long-term deafness per se (LDU group) results in a significant decrease in BRRs [median 6 + 1 (Q) pps] compared with the control group [median 12 + 2 (Q) pps; P < 0.01]. Following chronic-passive stimulation, BRRs of long-deaf animals [LDS(−) group] significantly increase [median 10 + 2 (Q) pps] compared with group LDU (P < 0.01). Additional behavioral training of long-deaf animals [LDS(+) group] results in a significant additional increase in BRRs [median 16 + 4.3 (Q) pps] compared with groups LDU and LDS(−) (P < 0.01). Also, BRRs in LDS(+) animals are equivalent to those obtained in control animals.

The comparisons of median cutoff rates in Fig. 4F demonstrate trends similar to those described for BRRs (Fig. 4C), with the exception that chronic-passive stimulation in long-deaf animals [LDS(−) group] does not result in a significant increase in cutoff rates [median 16 + 3 (Q) pps] compared with the LDU group [median 10 + 1 (Q) pps; P > 0.05]. Cutoff rates in the LDU group are significantly lower than those in the control group [median 22 + 5 (Q) pps; P < 0.01]. Following behavioral training, LDS(+) animals demonstrate a significant increase in cutoff rates [median 24 + 7 (Q) pps] compared with LDU and LDS(−) animals (P < 0.01 and P < 0.05, respectively). Cutoff rates in LDS(+) animals are virtually identical to those in control animals (P > 0.05).

In summary, these results indicate that long-term deafness (LDU group) results in degraded temporal following (i.e., lower BRRs and cutoff rates) compared with both control and behaviorally trained animals. Chronic-passive stimulation [LDS(−) group] modestly improves temporal following (BRRs) compared with long-deaf unstimulated animals (LDU group). In contrast, increased temporal following (BRR and cutoff rate) in behaviorally trained animals [LDS(+) group] is equivalent to temporal following in control animals and is significantly higher than temporal processing observed in the LDU and LDS(−) groups, as illustrated in cumulative probability functions and by statistical analyses.

Temporal processing: peak latency. Temporal processing properties were assessed further by examining the peak latencies of AI neurons in response to a single electric pulse. The peak latency is defined as the modal latency in the period histogram for a stimulus frequency of 2 pps (stimulus duration 500 ms; Fig. 2, C and D). Figure 5A shows the quantitative distribution of peak latencies for the four groups of animals. The distributions of peak latencies for the control and LDS(+) animals are closely overlapping and shifted towards shorter latencies compared with the distributions for the LDU and LDS(−) animals.
animals have a median peak latency of 10.4 ± 0.7 (Q) ms. Long-term deafness per se (LDU animals) results in a significant increase in peak latency to a median of 12±1.5 (Q) ms ($P < 0.05$). Chronic-passive stimulation of long-deaf animals without behavioral training [LDS($-$) group] does not alter peak latencies compared with LDU animals ($P > 0.05$), and the latencies in LDS($-$) animals [median 13 ± 1.5 (Q) ms] are significantly longer than those in both the control and LDS($+$) groups ($P < 0.05$ and $P < 0.01$, respectively). In contrast, behavioral training [group LDS($+$)] results in latencies [median 11 ± 1.63 (Q) ms] that are significantly shorter than those in both LDU and LDS($-$) animals (both $P < 0.01$). Following behavioral training, the peak latencies of LDS($+$) animals are essentially equivalent to values observed in previously normal hearing control animals ($P > 0.05$).

A linear regression analysis between BRRs and peak latencies was performed for recording sites in each of the four groups of cats. In LDS($+$) cats, a significant inverse correlation ($R = 0.11$, $P = 0.002$, 95% confidence interval) between BRRs and latencies is found, i.e., as BRRs increase, latencies significantly decrease. Application of a Bonferroni correction for multiple comparisons indicates no significant correlations between BRRs and latencies in the other three groups of animals (Bonferroni required $P = \alpha/4 = 0.05/4 = 0.0125$).

**Temporal precision: minimum latency and jitter.** To examine the temporal precision of cortical responses to electric stimulation, we determined the mean onset time of the first spikes (mean minimum latency) and their timing variability or jitter, as expressed by the SD of minimum latencies over all repetitions in response to a single biphasic pulse (pulse rate of 2 pps, sweep duration of 500 ms). The dot raster histograms in Fig. 6, A and B, are derived from the same neurons as shown in Fig. 2, A and B, and show exemplary neuronal responses in a LDU animal (Fig. 2A) and a LDS($+$) animal (Fig. 2B). The open circles indicate the minimum latencies of responses for each stimulus repetition within a physiological time window (7–28 ms, grey frame). In the given examples, the average mean minimum latency recorded in the LDS($+$) animal is shorter (7 ms), and the jitter is lower [±0.95 (SD) ms] than those for the equivalent responses recorded in the LDU animal [latency: 9.4 ms, jitter: ±1.47 (SD) ms].

Figure 6, C and D, shows the statistical comparisons of the average mean minimum latencies (Fig. 6C) and the average jitter of the minimum latencies (Fig. 6D) for the four experimental groups (one-way ANOVA, $P < 0.001$, Holm-Sidak pairwise multiple comparison). Cortical neurons in the LDU group have significantly longer mean minimum latencies [mean 11.34 ± 1.38 (SD) ms] and higher jitter [mean 1.44 ± 0.74 (SD) ms] than those in the control group [latency: mean 8.46 ± 0.70 (SD) ms, jitter: mean 1.03 ± 0.60 (SD) ms; $P < 0.01$], indicating degraded spike timing and decreased temporal precision after long-term deafness. Chronic-passive stimulation of long-deaf animals [LDS($-$) group] has no effect on either mean minimum latency or jitter [latency: mean 11.54 ± 1.13 (SD) ms, jitter: mean 1.33 ± 0.61 (SD) ms] compared with the LDU animals (both $P > 0.05$). However, group LDS($-$) has significantly longer minimum latencies compared with minimum latencies in the control and LDS($+$) groups (both $P < 0.01$). In agreement with the results for the peak latencies measures, behavioral training [LDS($+$) group] results in significantly shorter mean minimum latencies [mean 9.25 ±
Comparison between short-deaf juvenile and long-deaf animals. In a previous report (Beitel et al. 2011), a similar study design was used to identify passive and training stimulation effects in neonatally deafened animals after <1 yr of deafness (short-deaf juvenile cats; average deafness duration 38 wk; mean SGC survival = 45% of normal). In that study, temporal processing in the AI was compared between short-deaf juvenile cats (group J300/30) that received only chronic-passive intracochlear electrical stimulation (300/30 SAM) and short-deaf juvenile cats that received additional training on detection of temporally modulated intracochlear electrical signals (group JT300/30). In the short-deaf juvenile groups, chronic stimulation and training histories were similar to those of corresponding long-deaf groups LDS(−) and LDS(+), included in the present study. The results showed that BRRs and cutoff rates in the behaviorally trained short-deaf cats were significantly higher than those recorded in short-deaf cats that received only chronic-passive stimulation. Moreover, behavioral training restored the temporal following ability to that observed in prior normal-hearing, adult deafened animals.

To discern the effects of longer term deafness on the efficacy of training-induced plasticity, we compared the temporal following ability of AI neurons between the short-deaf and long-deaf animals in the two studies (Mann-Whitney rank sum tests). Comparisons of the BRRs and cutoff rates between the passively stimulated groups J300/30 and LDS(−) revealed no difference (Fig. 7A; both P > 0.05). Corresponding comparisons between the two behaviorally trained groups JT300/30 and LDS(+) demonstrate significantly higher BRRs and cutoff rates in the long-deaf LDS(+) animals (Fig. 7B; P < 0.001 and P < 0.01, respectively). Furthermore, in contrast to the decreases in peak and minimum latencies in the behaviorally trained long-deaf animals [LDS(+) group] reported in the present study, Beitel et al. (2011) did not observe training-induced changes in latencies in the short-deaf animals. These results demonstrate that long-term deafness does not have a limiting influence on the efficacy of training-induced plasticity compared with short-term deafness. In fact, the comparisons suggest that the effect of behavioral training is even stronger after long-term deafness.

DISCUSSION

The present study indicates that prolonged durations of early onset deafness produce profound deficits in the representation of temporally modulated electric pulse trains in AI neurons. We found that the introduction of auditory experience resulted in changes in temporal processing that were dependent upon the behavioral context of the auditory input. Chronic-passive electric stimulation had a moderate impact on temporal following (BRR) but otherwise had no effects on timing or temporal response precision in AI neurons. In contrast, despite the complete lack of any auditory experience before electric hearing onset until adulthood, electrical stimulation associated with behavioral training and perceptual learning had a much more pronounced effect on cortical temporal processing in long-deaf animals and markedly enhanced the spike-timing precision and the capacity of AI neurons to temporally resolve successive auditory inputs. Indeed, with the exception of minimum latencies, behavioral training of developmentally deafened adult...
effects of long-term deafness and electric auditory experience on cortical temporal processing. Our results are consistent with earlier studies in hearing animals demonstrating that manipulations of normal acoustic input during development by postnatal exposure to structured noise resulted in degraded cortical temporal processing capacities as expressed by lower peak and minimum response latencies and reductions in both peak and minimum response latencies and spike latency variability were only observed in animals trained untrained, shock-matched control animals. However, improve-ments in the precision of spike-timing as expressed by the first spike latency variability were only observed in animals trained in the avoidance task. In the present study, the training-induced reductions in both peak and minimum response latencies and critical period juvenile and adult animals (Bao et al. 2004; Beitel et al. 2003; Zhou and Merzenich 2008, 2009). Thus a critical period for the ability to reorganize temporal response properties of auditory cortex may not exist. Changes in temporal processing may mainly be dependent on the specific sensory input and its behavioral significance (Ahissar and Ahissar 1994) when applied at any age. Another possibility is that degrading or eliminating auditory input during development may extend the critical period for temporal plasticity into adulthood as suggested for the spectral representation of acoustic signals in rats reared in continuous noise (Chang and Merzenich 2003).

These assumptions are strengthened by a comparison of the present study with recent findings in profoundly deaf juvenile cats. Using a comparable training design, Beitel et al. (2011) reported a significant increase in the temporal following ability of AI neurons in neonatally deafened juvenile cats. Surprisingly, despite the significantly shorter deafness durations and higher SGC survival, training-induced enhancements in temporal following ability in these animals remained significantly below that of behaviorally trained long-deaf animals [LDS(+)] group]. These findings underscore that the potent efficacy of training-induced temporal plasticity is not limited by long-term deafness and its deleterious effects on peripheral (e.g., Leake and Hradek 1988; Vollmer et al. 2007) and central morpholog (e.g., Leake et al. 2008; Lustig et al. 1994; Nishiyama et al. 2000).

As there were no consistent differences in the stimulation or training strategies between the two studies, intrinsic differences have to be assumed and require future investigations. One possibility is that due to the severe degeneration of the afferent neural population in LDS(+) animals, electrical stimul-i may elicit highly synchronous inputs across relatively broad sectors of the cochlea, thereby eliciting a particularly powerful effect on temporal response properties.

Experience- or learning-induced plasticity of cortical response latencies has not been widely studied. In a model of cortical activity, Egggermont and Ponton (2002) suggested that input synchrony based on peripheral mechanisms influences response latency and jitter in auditory cortex. However, learn-ing-induced changes in latencies of AI neurons are difficult to interpret because experimental results from earlier studies are not consistent. For example, following temporal discrimination training Bao et al. (2004) did observe increased cortical temporal filter frequencies but no changes in response latencies. Similar results are reported in a contemporary study on the effects of behavioral training in neonatally deafened juvenile cats (Beitel et al. 2011). Following frequency discrimination training in brown monkeys, Recanzone et al. (1993) reported increases in first spike latencies of cortical neurons, whereas in cats a decrease in latencies was reported (Brown et al. 2004). Using an avoidance-conditioning paradigm for a single tone detection task in rats, Leon et al. (2008) documented increased average first spike latencies in response to noise but not to a pure-tone stimulus. In contrast, peak latencies were reduced relative to naïve animals, an effect that was also observed in untrained, shock-matched control animals. However, improve-ments in the precision of spike-timing as expressed by the first spike latency variability were only observed in animals trained in the avoidance task. In the present study, the training-induced reductions in both peak and minimum response latencies and...
improvements in spike-timing precision were paralleled by increases in cortical temporal following (BRR and cutoff rates). Similar effects were not observed in passively stimulated or unstimulated long-deaf animals. With the exception of minimum latencies, in behaviorally trained long-deaf animals all of the parameters tested were restored to levels equivalent to those recorded in prior normal hearing control animals.

Only a small number of studies have demonstrated changes in cortical temporal processing following passive stimulation (e.g., Kim and Bao 2009; Leon et al. 2008). The present study also showed an effect of passive stimulation on a single parameter for temporal processing (BRR), whereas all other parameters tested were exclusively affected by behavioral training. Thus our results confirm the findings of the majority of previous studies that focused attention on behaviorally relevant sensory events required to drive cortical plasticity, whereas passive sensory stimulation fails to induce plastic changes in cortical temporal processing (Bao et al. 2004; Beitel et al. 2011; Zhou and Merzenich 2009).

The present results from auditory cortical neurons are consistent with earlier electrophysiological studies in cat auditory midbrain demonstrating that long-term deafness per se resulted in degraded temporal processing (lower maximum following frequencies, longer first spike latencies) in ICC neurons (Snyder et al. 1995; Vollmer et al. 2005), whereas chronic electric (higher rate) stimulation significantly increased temporal processing in ICC neurons even after long periods of complete auditory deprivation. However, the results in these earlier studies were not separately analyzed for long-deaf animals that received only chronic-passive stimulation alone and those that received additional behaviorally relevant training. A more recent direct comparison of experience-induced changes in temporal processing between ICC and AI found that behavioral training and perceptual learning significantly enhanced cortical temporal following ability in long-deaf cats, whereas in the ICC of the same cats there was no evidence that improvements in temporal following were behaviorally modulated (Vollmer and Beitel 2010). These findings suggest that behavioral training is not required to drive changes in temporal processing on the level of the auditory midbrain. Instead, in the adult, long-deaf auditory system, auditory midbrain neurons are influenced by auditory input signals that are not behaviorally relevant. In contrast, AI neurons demonstrate a strong capacity for perceptual learning-induced improvements in temporal processing that is clearly superior to temporal processing produced by unattended, chronic-passive stimulation alone.

Earlier psychophysical studies indicate that detection and discrimination of electric pulse trains are based on detection of the peak amplitude of the temporally modulated signals (Beitel et al. 2000b; Vollmer et al. 2001). With respect to the present study, the effective stimulus parameter for behavioral detection and neural plasticity was the peak amplitude of the temporally modulated pulse trains, either 30 or 300 pps modulated sinusoidally at 30 Hz. Modulation at a rate of 30 events/s is challenging for AI neurons to encode and represent in a phase-locked manner, given their normal BRR of 8–15 Hz (Beitel et al. 2003; Joris et al. 2004; Schreiner and Raggio 1996). The changes in cortical temporal processing observed in this study are likely produced by the statistical properties of the stimuli and the scheduling or pairing of the signals with reinforcement during behavioral training. Discrimination or identification of specific temporal cues associated with the signals are not required for cortical temporal plasticity to occur (Beitel et al. 2011; Kilgard et al. 2001). Future studies using a larger variety of temporally modulated signals are needed to confirm stimulus-rate specific alterations in cortical temporal processing and to identify stimulus parameters that are best suited to enhance temporal processing in AI.

Potential mechanisms. The specific mechanisms that enable cortical field AI to adjust temporal processing of auditory information in response to behavioral training and perceptual learning remain largely unknown. Potential mechanisms include changes in auditory cell intrinsic characteristics, sensory cortical synaptic properties, and intracortical network dynamics or “top-down” influences.

The loss of myelin observed after long-term deafness may lead to an increased membrane capacitance (Koles and Rasminsky 1972; Tasaki 1955) that could reduce the efficiency of a neuron in response to electric stimuli and increase the likelihood of a conduction block. Also associated with the loss of myelin and partial neural degeneration are prolonged refractory periods and an increased vulnerability of the propagating spike (Cragg and Thomas 1964; Felts et al. 1997; Koles and Rasminsky 1972; McDonald and Sears 1970; Shepherd and Javel 1997; Smith and McDonald 1999; Tasaki 1955). The resulting reductions in the transmission of afferent spiking activity may result in diminished synaptic efficacy and thus contribute to lower temporal resolution and increases in response latency and jitter as observed in the long-deaf, unstimulated animals (group LDU).

It is likely that the behaviorally induced modulations in temporal processing described in our results are based at least partially on changes in synaptic strength that occur within the auditory sensory cortex. The underlying mechanisms may include local Hebbian-type synaptic processes (Cruishank and Weinberger 1996; Diamond et al. 1993), changes in the synaptic organization or strength of existing intrinsic circuits (e.g., modification in synaptic size or relocation of synapses to more effective sites on the target neuron), sprouting of new afferents that results in increased synaptic density, and/or alterations in membrane properties (e.g., Eysel 1981; Kaas 1996; Keller 1990). Each of these mechanisms could lead to improved synaptic efficacy and higher synchrony in the neuronal excitation pattern resulting in an increase in the temporal resolution and precision of AI neurons.

Another consideration for our results is that auditory deprivation and behaviorally relevant auditory experience may differentially affect the balance of excitation and inhibition in AI (e.g., Chen and Jen 2000; Schreiner and Raggio 1996; Wang et al. 2002). Behavioral training may result in alterations in the synaptic time constants via shortened cortical postexcitatory suppression, greater and earlier postdepression facilitation, and changes in slow inhibitory potentials (Bao et al. 2004; Joris et al. 2004; Markram and Tsodyks 1996; Mauk and Buonomano 2004; Zhou and Merzenich 2009). These factors likely improve cortical response dynamics and support faster cycle-by-cycle processing. In addition, recent results from in vivo whole cell recordings suggest that synaptic inhibition and synaptic depression are involved in postexcitatory suppression (Tan et al. 2004; Wehr and Zador 2003, 2005). Changes in the interaction of synaptic excitation and inhibition may result in modifications in the time course of spiking activity in AI neurons and.
thus, be a potential mechanism for behaviorally induced temporal plasticity reported in this study.

The diverse effects of auditory experience and behavioral training on enhanced temporal cortical processing are likely mediated by multiple neuromodulatory systems. For example, cholinergic activation can enhance the representation of higher-rate stimuli (Kilgard and Merzenich 1998; Kilgard et al. 2001). The release from N-methyl-d-aspartate-receptor-mediated GABAergic inhibition or blocking GABAergic receptors in auditory cortex results in facilitation of the late excitatory postsynaptic potential and in increased response strength and shorter latencies (Chen and Jen 2000; Metherate and Ashe 1994; Wang et al. 2000). Both the cholinergic and the GABAergic systems are involved in the regulation of cortical plasticity and, likely, also contribute to stimulation- and learning-induced maintenance and alteration of temporal processing (Froemke et al. 2007; Weinberger and Bakin 1998). Other neurotransmitters may also contribute to experience-driven cortical plasticity (e.g., dopamine; Bao et al. 2001).

Overall, although the exact mechanisms and their potential interactions that underlie temporal plasticity are still largely unknown, our results indicate that behavioral training and perceptual learning are clearly more effective in adjusting and modulating the various processes that govern cortical temporal processing than chronic-passive electric stimulation.

Anesthesia. It is well known that barbiturate anesthesia affects cortical responsiveness. However, the expression of behaviorally driven neuroplasticity in primary auditory cortex is not prevented by anesthesia. All of the neuronal responses reported in the present study were recorded from animals that were barbiturate-anesthetized following a strict protocol designed to maintain a surgical level of anesthesia. Given the significant differences in temporal processing and neural plasticity among the four groups of animals, it is likely that differences in hearing experience rather than anesthesia are responsible for the observed effects.

Conclusions. Our results indicate that behavioral training and perceptually relevant auditory experience have a powerful potential to adjust and enhance profoundly degraded cortical temporal processing in the deaf adult auditory system deprived of all acoustic and electric hearing experience starting before the onset of hearing and continuing over long periods of time.

Because the ability to encode and resolve the temporal patterns of complex electric signals is crucial for speech recognition performance of cochlear implant subjects (e.g., Eddington et al. 1978; Fu 2002; Shannon 1992; Townsend et al. 1987; Wilson et al. 1991), the present study has important clinical implications. The described improvements in cortical temporal processing may be a physiological correlate for perceptual training-induced improvements in speech perception and language-processing abilities. Our results are concordant with clinical studies that confirm the effectiveness of auditory training for speech perception in both pediatric and adult cochlear implant users (e.g., Boothroyd 2010; Chen et al. 2010; Fu and Galvin 2007; Oba et al. 2011; Stacey et al. 2010), and they are consistent with studies that suggest a capacity of the developmentally impaired auditory system for functional reorganization and restoration even in older children and adults (Merzenich et al. 1996; Tallal et al. 1996).

Although the present results show that the efficacy of training-induced temporal plasticity is not dependent on the duration of deafness, clinical studies demonstrate a negative correlation between deafness duration and speech discrimination performance. Clearly, additional factors other than temporal processing (e.g., spatial resolution of electric signals, competing signals and noise) affect speech discrimination performance. Although it has been shown at the level of the inferior colliculus that the degradation in spatial selectivity after long-term deafness is not reversible (Vollmer et al. 2007), the effect of behavioral training on spatial signal representation in auditory cortex still has to be investigated.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

M.V. and R.E.B. conception and design of research; M.V. and R.E.B. performed experiments; M.V. and R.E.B. analyzed data; M.V. and R.E.B. interpreted results of experiments; M.V. prepared figures; M.V. drafted manuscript; M.V. and R.E.B. edited and revised manuscript; M.V. and R.E.B. approved final version of manuscript.

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