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Research paper

Disappearance of contralateral dominant neural activity of auditory cortex after single-sided deafness in adult rats

Min Young Lee[a,b,c,1], Doo Hee Kim[a,d,1], Su-Kyoung Park[e], Sang Beom Jun[f], Yena Lee[f], Jun-Jae Choi[a], Hyun Ji Yoo[f], Yehoash Raphael[b], Seung-Ha Oh[a,g,*]

[a] Department of Otorhinolaryngology-Head and Neck Surgery, Seoul National University Hospital, Republic of Korea
[b] Kresge Hearing Research Institute, Otolaryngology - Head and Neck Surgery, The University of Michigan Medical School, United States
[c] Department of Otorhinolaryngology-Head and Neck Surgery, Dankook University Hospital, Republic of Korea
[d] Interdisciplinary Program in Brain Science, College of Natural Sciences, Seoul National University, Republic of Korea
[e] Department of Otorhinolaryngology-Head and Neck Surgery, Hallym University Medical Center, Republic of Korea
[f] Department of Electric and Electrical Engineering, Department of Brain & Cognitive Sciences, College of Engineering, Ewha Womans University, Republic of Korea
[g] Biomedical Research Institute, Seoul National University Hospital, Republic of Korea

HIGHLIGHTS

- Adult rats show plastic changes of both brain hemispheres after single side deafness.
- The plastic change can be summarized as the loss of normal contralateral dominance.
- Serial time point analysis suggests the two different phase after single side deafness.

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ABSTRACT

Hearing loss in mature ears can cause functional reorganization of the auditory cortex. The functional reorganization is speculated to negatively affect the outcome of hearing rehabilitation. Therefore, once hearing loss occurs, it is important to provide auditory input before extensive reorganization in the auditory pathways. We investigated the neural plasticity in auditory cortex after single-sided deafness (SSD) in an adult rat model. The animals were divided into two groups: a normal hearing (NH) and the SSD group. The neural recordings of the SSD group were conducted at different time points (2, 4, 6 and 8 weeks) after cochlear ablation. The multi-unit activity was discriminated on the sum of spikes, peak amplitude, onset latency, peak latency, and responsive area based on the peak amplitude. The auditory cortical reorganization was observed after SSD. The contralateral dominance of peak amplitude and latency that normally occur in NH group were not present in the SSD group, replaced by higher amplitude and faster response in ipsilateral cortex. According to serial recordings at different time points after SSD, different phases in the response of the auditory cortex were speculated. Compared with normal hearing, alteration of contralateral dominance was observed because of the functional reorganization of the auditory cortex after SSD.

1. Introduction

The activation of contralateral auditory pathway after monaural sound stimulation is thought to be more dominant than the ipsilateral pathway in the central auditory system of normal hearing (NH) mammals [2,8]. The contralateral pathway has a greater number of nerve fibers, fewer synapses, and direct connection than the ipsilateral [1,5,9]. These results are supported by physiological studies in mammals [15,26,29] and also by human studies [25] using magnetoencephalography [10,23,30,36] and functional

* Corresponding author at: Department of Otorhinolaryngology-Head & Neck Surgery, Seoul National University College of Medicine, Seoul 110-744, Republic of Korea.
E-mail address: shaoh@snu.ac.kr (S.-H. Oh).
[1] These authors have contributed equally to this paper.

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magnetic resonance imaging [32], confirming the presence of contralateral dominance of the central auditory pathway.

Cortical neural development of the auditory pathways is dependent on sound stimulation [19]. The absence of acoustic input can lead to abnormal auditory neural development and connectivity, and result in a delay of language development in childhood [19]. Similarly, complete loss of the acoustic input after cortical development can cause functional reorganization of the central auditory pathway in mature auditory cortices. This functional reorganization after the loss of hearing could affect the outcome of hearing and speech performance when the hearing is restored by cochlear implant or other hearing rehabilitation approaches. The extent and timing of this functional reorganization after a hearing loss in mature mammals are still unclear.

Unilateral deafness, as well as bilateral deafness, is considered as an indication of cochlear implant recently. Therefore, the importance of research on the single-sided deafness (SSD) to optimize the clinical outcome is emphasized [6]. Functional reorganization of auditory cortices has been shown after congenital or early life SSD [17,18]. In contrast to early life reorganization and functional changes, less plasticity is expected in the adult auditory cortices, as critical periods for brain plasticity decline with age [4,27,37]. Nevertheless, several recent reports of human imaging studies have indicated that there are functional and structural changes after SSD in adulthood [7,20,21].

There are various methods to monitor the neural activity evoked by auditory stimulation. The multi-unit recording allows simultaneous recording from multiple neurons, an analysis of different neural response patterns and the interactions among neurons with high spatial and temporal resolutions [33]. Several studies used the method and investigated the neural activities in non-auditory fields successfully. We observed the neural activity of bilateral auditory cortices in NH and SSD adult animals using the multi-unit recording. By comparing selected parameters of the peri-stimulus time histogram (PSTH) and responsive area of both auditory cortices between NH and SSD animals, we demonstrate alteration of contralateral dominance which was observed in normal hearing subjects, showing progressive enhancement of neural activity of the ipsilateral auditory cortex.

2. Materials and methods

2.1. Animal preparation

Experiments were performed on 26 adults female Sprague–Dawley rats (250–500 g; 6 weeks old at the beginning of the study). Experiments consisted of two parts. In part I, experiments were performed on 5 NH and 17 SSD rats. Each parameter acquired by extracellular recording from the bilateral brain cortices was compared between the NH and SSD group. In part II, the SSD rats were divided into four subgroups according to the duration of unilateral hearing deprivation. The recording was performed at 2 (SSD 2wk, n = 4), 4 (SSD 4wk, n = 5), 6 (SSD 6wk, n = 3), and 8 (SSD 8wk, n = 5) weeks after cochlear ablation.

Baseline ABR was measured to exclude the animals with hearing loss. For the NH group, the deafening procedure was not performed. After the recording, animals were sacrificed. For the SSD group, left-sided cochlear ablation [22] was performed at 7 weeks of age. The experimental age was determined in consideration of the lifespan and cochlear maturation [33]. A postauricular incision was made after anesthesia with an intramuscular injection of a mixture of tiletamine/zolazepam (30 mg/kg) and xylazine (5 mg/kg). Atropine sulfate (0.22 mg/kg, i.m.) was injected to reduce the bronchial secretions and dexamethasone (0.25 mg/kg, i.m.) was injected to decrease brain swelling and edema. The body temperature was maintained at 36–37 °C to prevent hypothermia. The cochlea was visualized using a surgical microscope (Carl-Zeiss, Oberkochen, Germany) at the medial portion of the bulla. The bony wall of basal turn of the cochlea was disrupted using a 26-gauge needle, and saline was irrigated through the perforation. The auditory brainstem response (ABR) was recorded 12 ms from the stimulus onset, and swept 512 times while stimulating each ear with click sound (rate: 19.1/s) in 5 or 10 dB SPL step using a Smart EP (Intelligent Hearing Systems, Miami, FL, USA). The ABR threshold was determined when the wave I to V disappeared. The hearing thresholds of the NH and SSD (lesion side) ears were <35 dB SPL and >80 dB SPL, respectively.

All procedures in this study were approved by the Seoul National University Institutional Animal Care and Use Committee (14-0152-C2A1). These animals were acclimatized in the breeding room for 1 week before the initiation of the experiment. The animals were cared according to the guidelines of the International Association for the Study of Pain in conscious animals [39].

2.2. Extracellular multi-unit recording of sound-evoked neural activity

The animals were anesthetized and shaved before surgery for bilateral auditory cortex exposure. A craniotomy was made over both temporal cortices spanning from Bregma to Lambda, and the auditory cortex surface area was identified based on the vascular pattern [14]. The dura mater was removed carefully using a 26-gauge needle and forceps. A screw was fixed to the parietal skull as a reference electrode. After fixation of the animal in the stereotaxic frame, a tungsten wire-based 16 channel microelectrode arrays (4 × 4 array, diameter: 35 μm, interelectrode spacing 500 (or 600) μm, 45° angled tip, impedance 300 kΩ @ 1 kHz in PBS (Innovative Neurophysiology, Inc., Durham, NC, USA)) was inserted perpendicular to the surface of the auditory cortex to a depth of 700–900 μm (target layer IV). To cover the primary auditory cortex, penetration was performed four times (total of 64 electrode penetrations) in each hemisphere (Fig. 1A, B). Gaussian white noise (80 dB SPL, 100 ms duration) was generated (TDT, Inc., Alachua, FL, USA) and introduced 200 times to the right ear every 685 ms during the recording in the bilateral auditory cortices.

2.3. Data processing and parameters

The waveform of neural activity was amplified 1000 times and filtered at 100–8000 Hz. Spike detection and sorting were performed using RASPUTIN and Offline Sorter™ (Plexon Inc., Dallas, TX, USA). The unit feature extraction was based on principal component analysis of spike sorting.

The units were classified using the T-distribution E-M clustering algorithm, and the artifacts were removed. After the automated sorting, visual inspection was performed manually to exclude unscreened artifact. The signal was obtained from multi-units rather than well sorted single-unit. Details in spike sorting process are provided in supplementary data 1.

Sorted files were processed in NeuroExplorer® (Plexon Inc.) to represent the neural activity changes to recursive events. Peristimulus time histograms (PSTHs) of the sound-evoked unit activity were generated and were optimized (observation period: 500 ms, time bin width: 3 ms, the number of trials: 200) according to the previous study [34]. We defined the responsive area as 'responsive' when the peak amplitude of PSTH was over 10 spikes/bin and synchronized (showing increased population of action potential at certain time bin after acoustic stimulus) with the stimulus.

To visualize and calculate the area responding to the sound stimulus, auditory cortex map was reconstructed using Voronoi tessellation method (MATLAB (MathWorks. Inc., Natick, MA, USA))