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Brain Research 724 (1996) 260–264

BRAIN RESEARCH

Short communication

A chronic microelectrode investigation of the tonotopic organization of human auditory cortex

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Accepted 12 March 1996

Abstract

We investigated the functional organization of human auditory cortex using a new chronic microelectrode technique. Tonotopic mapping data was obtained at the single unit level for the first time in humans. All sound-driven units were noted to have frequency-dependent response patterns. The majority of units (73%) demonstrated sharply tuned excitatory best-frequency responses. Twenty seven percent of units showed wide receptive fields, representing excitatory responses to almost the entire range of frequencies presented. A tonotopic pattern was observed with best frequencies systematically increasing as more medial-caudal recording sites were sampled.

Keywords: Human; Auditory cortex; Tonotopic representation; Microelectrode; Chronic; Single unit

Tonotopic organization within auditory cortex has been demonstrated experimentally in a variety of mammalian species, including nonhuman primates [7,10,11,20]. During experimental animal investigations, extensive use has been made of the technique of serial single unit microelectrode recordings followed by post-recording histological analysis. Complex tonotopic maps of primary and surrounding association auditory fields have been described using this investigative approach.

In contrast, prior physiologic studies of human auditory cortex have been carried out using methods incapable of recording the activity of individual cortical units. Field potentials have been recorded from macroscopic clinical depth electrodes placed in epilepsy surgery patients [2], or by using non-invasive methods such as magnetoencephalography (MEG) [4,12,16,17,19], electroencephalography (EEG), and positron emission tomography (PET) [8]. Using these methods, several investigators have demonstrated that electrical and magnetic field potentials, as well as blood flow changes from macroscopic regions of human auditory cortex display a simple tonotopic organization, with higher frequency tones activating more posterior-medial regions of auditory cortex [2,4,8,12,16,17,19]. Findings from a recent MEG study of human auditory cortex, however, suggest that a more complex tonotopic organizational pattern may exist [13].

In order to investigate this issue further, we studied the functional organization of human auditory cortex by examining the receptive field properties of many individual auditory cortex units. Using a recently described chronic microelectrode recording method [6], it was possible to determine the cellular basis for a tonotopic pattern in a human subject.

Chronic single unit microelectrode recordings were obtained using a recently developed hybrid depth electrode (HDE) technique [6] (Fig. 1). The HDE has the same external physical characteristics as a standard clinical depth electrode (1.25 mm OD), including three low impedance contacts for clinical EEG recordings. Six microelectrode recording sites are interspersed along the shaft of the macroscopic electrode and allow investigators to chronically record multi-unit activity from which single units can be discriminated [6]. HDEs are implanted in epilepsy

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PII S0006-8993(96)00315-0

surgery patients who require depth electrode placement as part of their standard clinical treatment plan. Use of the HDE instead of a standard depth electrode does not increase the surgical risk to the patient, and all experimental protocols have been approved by the University of Iowa Human Subjects Review Board.

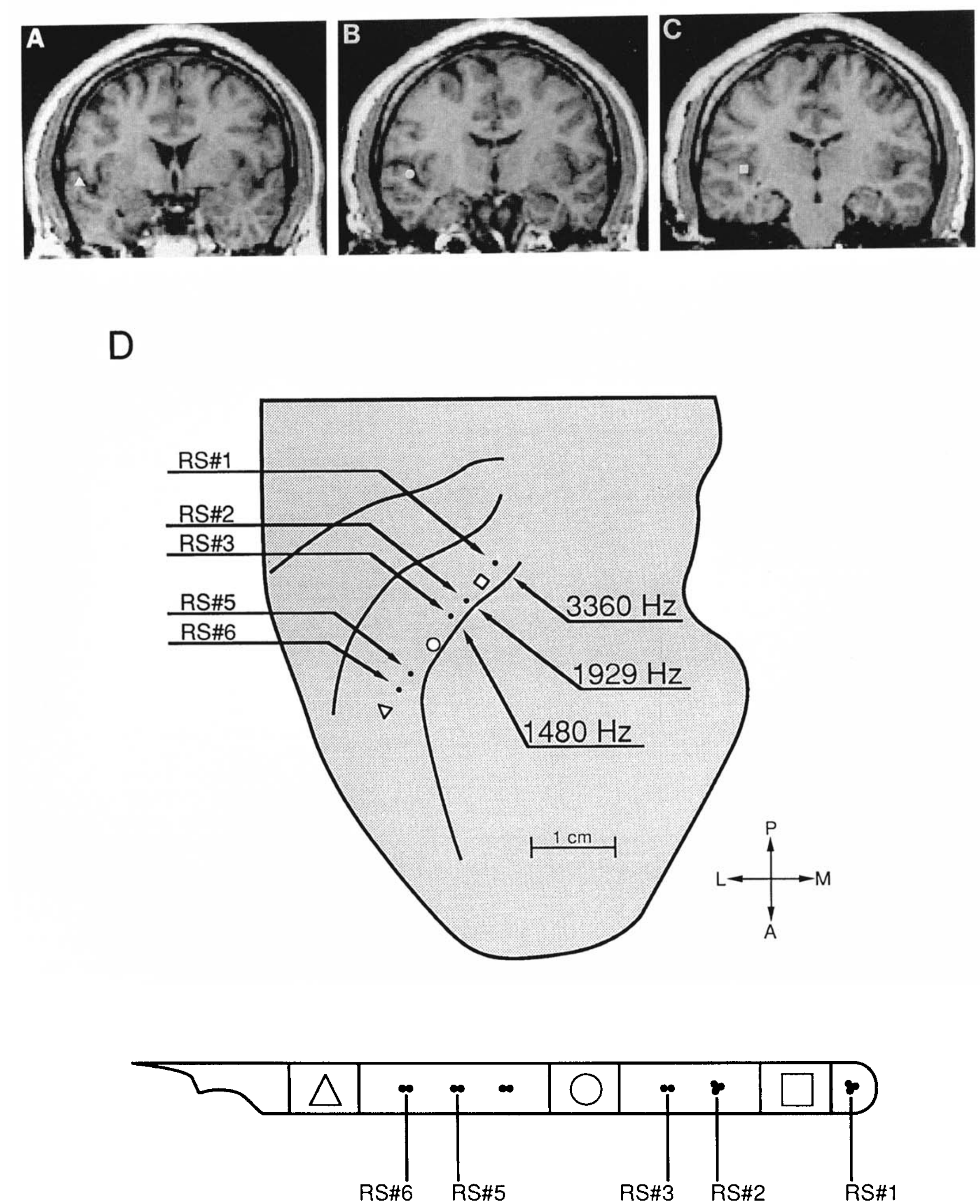

Fig. 1. Anatomical data demonstrating the location of HDE recording sites. The electrode configuration with three low impedance EEG recording contacts (triangle, open circle and square) and six microelectrode recording sites is depicted in the schematic diagram (D, lower). Coronal MRI images A (anterior), B (middle), and C (posterior) show the locations of the three EEG contacts within right-sided Heschl's gyrus. Locations of microelectrode recording sites 1, 2, 3, 5, and 6 are depicted in the line drawing of the patient's right sided planum temporale (D). This is a scaled tracing of a three-dimensional MRI image of the subject's brain obtained using Brainvox [3]. The suprasylvian cortex has been removed, thus providing an image of the exposed superior temporal plane as viewed from above. Units responsive to pure tone stimulation were recorded from sites 1, 2, and 3. Mean best frequencies for the units recorded at each site are indicated (L = lateral, M = medial, A = anterior, P = posterior).

In the current report, a HDE was placed into the right (non-dominant) Heschl's gyrus of a patient with medically intractable epilepsy and normal hearing. The electrode was placed stereotactically within grey mater, along the long axis of the gyrus. Following electrode implantation, and prior to removal of the stereotactic head frame, a head CT scan was obtained. The head frame was used to volume co-register the pre-operative MRI and post-operative CT scan brain images as previously described [6]. Electrode recording site CT imaging data was transferred to the MRI images as shown in Fig. 1. The data described was obtained during a tonotopic mapping experiment carried out 10 days after HDE implantation.

Isointensity (75 dB SPL) tones of 24 different frequencies (300-ms duration, 5-ms rise and fall times, range 200 to 10 000 Hz) were presented at 1-s intervals through an insert ear phone (Etymotic Research, Elk Grove Village, IL) placed in the patient's left ear. The time code from the sound stimuli and the amplified physiologic signals from the microelectrode recording sites were all stored on a multi-channel FM tape recorder (Racal, Irvine, CA). Action potentials from individual units were discriminated from multi-unit recording data using a threshold-slope window discriminator (F. Haer, Brunswick, ME). Peristimulus time histograms were generated using 10-ms time bins. Frequency response tuning curves to tone onsets were generated by comparing firing rates during the first 100 ms following tone onset with the background firing rate (300 ms prior to tone onset).

The post implantation electrode imaging data confirmed the location of a linear array of recording sites within Heschl's gyrus. These sites are oriented parallel to the long axis of the gyrus and are in close proximity to the first transverse sulcus (Fig. 1). Good quality bipolar microelectrode recordings were obtained from 5 of the microelectrode sites; recordings from site 4 were compromised by a dysfunctional electrode wire. Forty units were isolated for analysis (Table 1). Background multi-unit activity was characterized by many spikes of different amplitude, polarity and firing rate. The amplitude of single spikes varied from 10 to 150 μV and the average rate of firing in the absence of auditory stimulation was 3.7 ± 0.27 impulses/s (mean $\pm$ S.E.M.).

Clear responses to tonal stimulation were obtained from

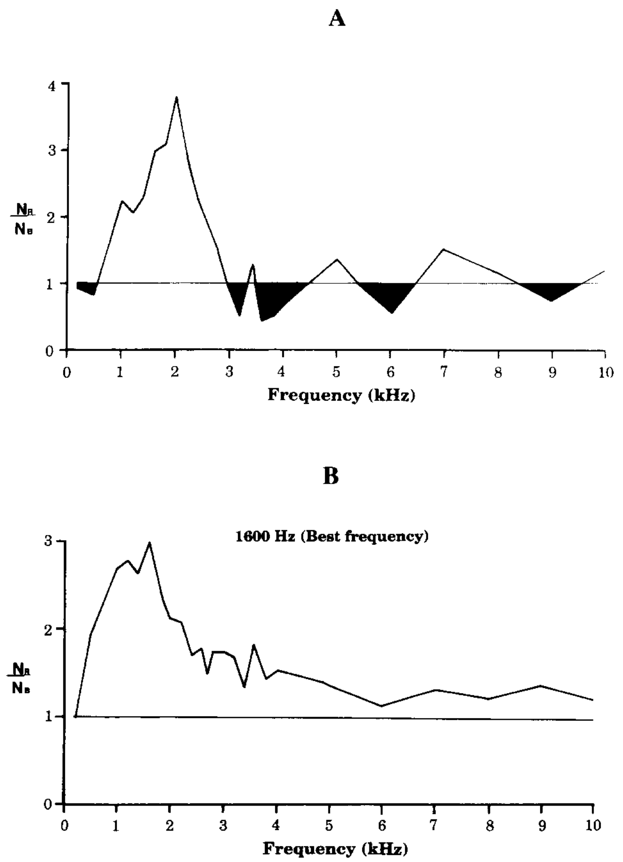

Fig. 2. Frequency tuning curves for auditory cortex units responding to pure tone stimulation (300 ms duration, 1 s interstimulus interval, 75 dB SPL. The unit shown in panel A displays a single-peak best-frequency (2000 Hz) with regions of surrounding inhibition; a pattern seen in 19 of 26 units (73%). In contrast, 7 units displayed a broad excitatory receptive field with no inhibitory responses, as shown in panel B. Abscissa: frequency (Hz) of the test tones. Ordinate: number of action potentials per second recorded during the first 100 ms following tone presentation (Nr), divided by the spontaneous activity (number of action potentials per second during the 300 ms preceding tone onset; Nb).

units recorded from microelectrode sites 1, 2, and 3. The distances along the electrode shaft separating these three recording sites from the point at which the electrode intersects the brain surface (superior temporal gyrus) are 32, 26 and 24 mm, respectively. The largest amplitude responses were obtained from sites 2 and 3. None of the

Table 1
Locations and auditory receptive field characteristics of human auditory cortex units

Microelectrode recording site number	Distance along electrode separating recording site from brain surface	Number of units studied	Number of units responsive to pure tone stimuli	Best frequencies (mean $\pm$ S.E.M. [Hz])
1	32	8	5	3360 ± 354.0
2	26	12	12	1937 ± 43.7
3	24	9	9	1489 ± 75.4
5	16	5	0	–
6	13	6	0	–

units recorded from sites 5 or 6 displayed responses to tone stimulation.

All sound-driven units were noted to have frequency-dependent response patterns. Some units displayed excitatory responses to some tone frequencies and inhibitory responses to other frequencies. Exclusively excitatory responses were noted in other, more broadly tuned units. A wide range of tone frequencies (400 to 4000 Hz) evoked responses in various units.

The majority of units (19 of 26, 73%) demonstrated sharply tuned excitatory best-frequency responses in conjunction with inhibitory responses to near-by non-best frequency tones (Fig. 2A). The excitatory receptive fields of the remaining units (7 of 26) were wide representing an excitatory response to almost the entire range of frequencies presented, and no inhibitory responses (Fig. 2B).

A variety of temporal response patterns to best-frequency stimulation were noted among the units studied (Fig. 3). Auditory responsive cortical units demonstrated initial response latencies ranging from 15 to 25 ms. Stimulation resulted in complex phasic and tonic responses to tone onsets in 19 units (Fig. 3A). Three of these nineteen also displayed phasic OFF responses (Fig. 3B). Tonic, slowly adapting responses were noted in 7 units (Fig. 3C).

The population of auditory cortex units studied displayed a tonotopic pattern of organization. The mean best frequencies for the units isolated at all recording sites are presented in Table 1. Mean best frequencies increased as the recording site position shifted more posteriorly and medially (1489, 1937, and 3360 Hz for recording sites 3, 2 and 1 respectively). The tonotopic data presented in this report were gathered ten days following electrode implantation. Mapping experiments where repeated on subsequent days, and no significant changes were noted in the tonotopic pattern.

Results of the present study demonstrate, for the first time, that individual human auditory cortex units respond to pure tone stimulation in a frequency-specific manner. The best-frequency responses for different populations of units positioned along the electrode's trajectory within Heschl's gyrus demonstrated a tonotopic pattern with higher best frequencies noted at more posterior-medial recording sites and lower best frequencies more anterior-lateral.

A wide range of individual human auditory unit response patterns to simple tones were noted. Some units had receptive fields characterized by a sharply tuned best frequency and surrounding inhibition while other units

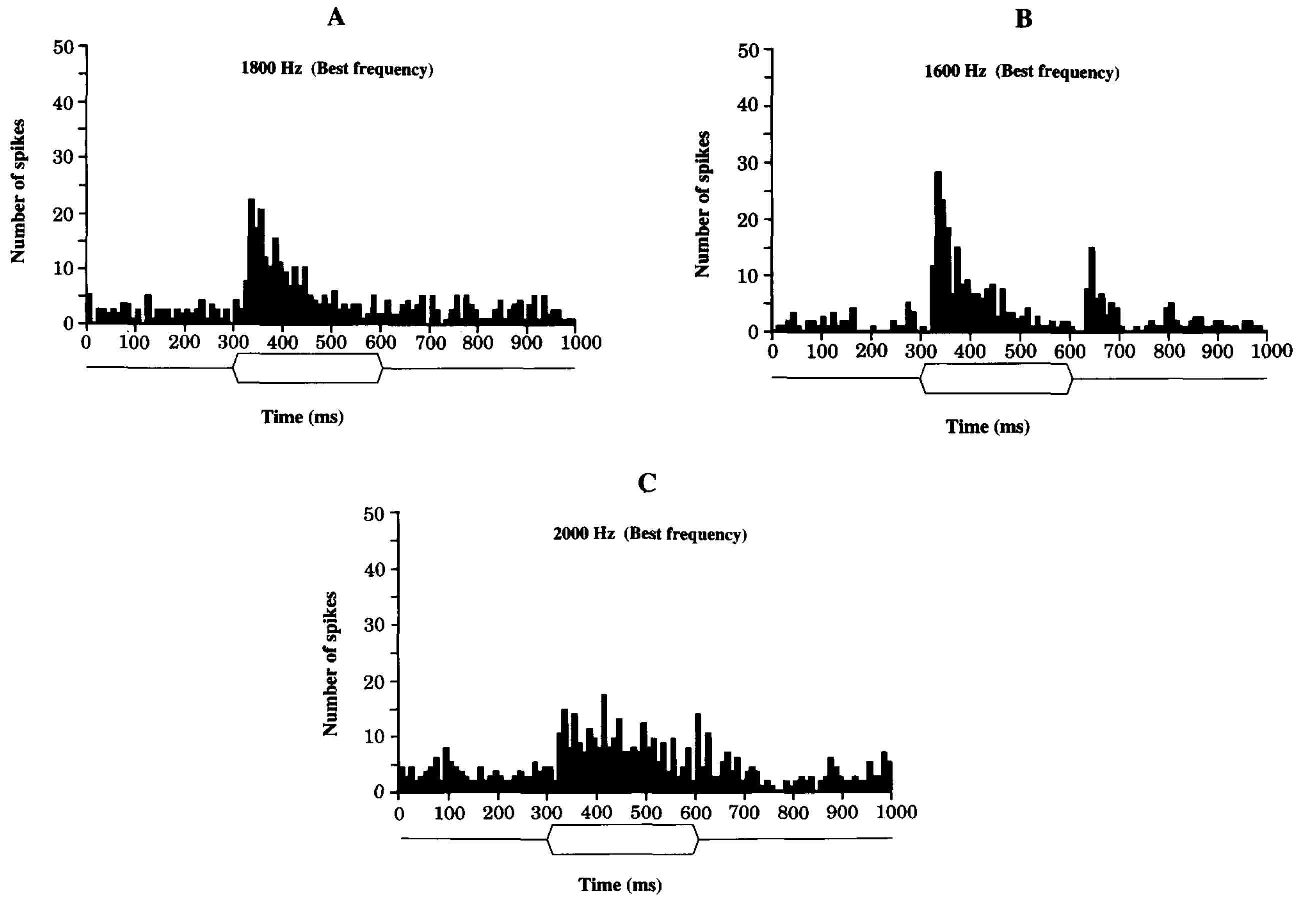

Fig. 3. Peristimulus histograms for three different units depicting a variety of temporal response patterns to best frequency stimuli. Nineteen units displayed complex phasic and tonic responses to tone onsets (panel A). Three of these 19 units displayed a phasic OFF response as well (panel B). A tonic, slowly adapting response, similar to that shown in panel C, was noted in 7 units.

were more broadly tuned with no regions of inhibition. These diverse receptive field characteristics are similar to those described previously in experimental animals [14,18,21,22]. Temporal responses to best-frequency stimulation also showed wide variability including phasic ON and OFF responses, and slowly adapting tonic responses to tone onsets. These temporal response patterns have been reported previously in experimental animal microelectrode investigations as well [1,21].

The human tonotopic pattern observed here is consistent with that previously described in monkey A1, with higher best frequencies located more posteriorly and medially [7,10]. This finding is also consistent with tonotopic patterns described in human MEG, PET and evoked potential studies [2,4,8,12,16,17,19]. The post-implantation imaging data confirms the location of recording sites within Heschl's gyrus, and earlier cytoarchitectural studies have shown that human Heschl's gyrus is composed of koniocortex consistent with primary auditory cortex [5,15]. Based on data obtained from a single line of sampling, however, it is not possible to conclude with certainty that the units studied were in human A1.

In monkey and cat, A1 is located within a small region of cerebral cortex surrounded by association auditory fields having their own tonotopic patterns of organization. Clear delineation of these distinct fields in experimental animals required extensive physiologic and anatomical investigation. That a similarly complex organization may exist in man is suggested by results of a recent MEG study demonstrating opposite tonotopic patterns, and different source localizations within human auditory cortex depending on the experimental parameters used [13]. In the current human experiment, an electrode placed in a different region of Heschl's gyrus, or in an adjacent transverse temporal gyrus might have disclosed a distinctly different organizational pattern.

Now that the feasibility of studying individual human auditory cortex units has been demonstrated, it should be possible to further clarify these complex physiologic issues with additional human experiments. This new investigative approach may also be very useful for examining issues of auditory cortex receptive field plasticity associated with complex human behaviors [9].

Acknowledgements

The authors thank Drs. Thomas Imig, Carolyn Brown and Bruce Gantz for their advice and assistance. This work was supported by grants from the Roy Carver and Hoover trusts.

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