THE JOURNAL OF COMPARATIVE NEUROLOGY 416:79–92 (2000)

Auditory Cortex on the Human Posterior Superior Temporal Gyrus

M.A. HOWARD,[1]* I.O. VOLKOV,[1] R. MIRSKY,[1] P.C. GARELL,[1] M.D. NOH,[1] M. GRANNER,[2] H. DAMASIO,[2] M. STEINSCHNEIDER,[3] R.A. REALE,[4] J.E. HIND,[4] AND J.F. BRUGGE,[4]

[1]Department of Surgery (Division of Neurosurgery), University of Iowa College of Medicine, Iowa City, Iowa 52242

[2]Department of Neurology, University of Iowa College of Medicine, Iowa City, Iowa 52242

[3]Departments of Neurology and Neuroscience, Albert Einstein College of Medicine, New York, New York 10461

[4]Department of Physiology and Waisman Center, University of Wisconsin, Madison, Wisconsin 53705

ABSTRACT

The human superior temporal cortex plays a critical role in hearing, speech, and language, yet its functional organization is poorly understood. Evoked potentials (EPs) to auditory click-train stimulation presented binaurally were recorded chronically from penetrating electrodes implanted in Heschl's gyrus (HG), from pial-surface electrodes placed on the lateral superior temporal gyrus (STG), or from both simultaneously, in awake humans undergoing surgery for medically intractable epilepsy. The distribution of averaged EPs was restricted to a relatively small area on the lateral surface of the posterior STG. In several cases, there were multiple foci of high amplitude EPs lying along this acoustically active portion of STG. EPs recorded simultaneously from HG and STG differed in their sensitivities to general anesthesia and to changes in rate of stimulus presentation. Results indicate that the acoustically active region on the STG is a separate auditory area, functionally distinct from the HG auditory field(s). We refer to this acoustically sensitive area of the STG as the posterior lateral superior temporal area (PLST). Electrical stimulation of HG resulted in short-latency EPs in an area that overlaps PLST, indicating that PLST receives a corticocortical input, either directly or indirectly, from HG. These physiological findings are in accord with anatomic evidence in humans and in nonhuman primates that the superior temporal cortex contains multiple interconnected auditory areas. J. Comp. Neurol. 416:79–92, 2000.

Indexing terms: auditory cortex; hearing; audition

The functional organization of auditory cortex has been studied extensively in a number of mammalian species, including nonhuman primates (for reviews see Bonin and Bailey, 1947; Bailey et al., 1950; Brugge, 1982; FitzPatrick and Imig, 1982; Aitkin, 1990; Brugge and Reale, 1985; Suga, 1988; Clarey et al., 1992; Kaas and Hackett, 1998; Rauschecker, 1998a,b; Schreiner, 1992, 1998). In the human, however, we still have only a rudimentary understanding of the functional organization of this part of the brain, despite knowing for more than a century that the cortex on the superior temporal gyrus (STG) plays a critical role in hearing, speech, and language. There is general agreement that in humans the primary auditory field (AI) is located deep within the lateral fissure on a small patch of the transverse gyrus of Heschl (HG) having distinctive cyto- and myelo-architectonic features (Flechsig, 1896; Vogt, 1903; Campbell, 1905; Brodmann, 1909; Economo, 1929; Bailey and Von Bonin, 1951; Hopf, 1964; Galaburda and Sanides, 1980; Seldon, 1981, 1985), that it is tonotopically organized (Pantev et al., 1988, 1995; Howard et al., 1996a; Lütkenhöner and Steinsträter, 1998), and that it exhibits auditory-evoked responses having latencies shorter than those recorded from more lateral sites (Liegeois-Chauvel et al., 1991, 1994). There is far less

Grant sponsor: The Hoover Fund; Grant sponsor: Carver Trust; Grant sponsor: Beth Abraham Hospital Institute for Music and Neurological Function; Grant sponsor: NIH; Grant numbers: DC00120, DC00657, DC00116, and HD03352.

*Correspondence to: Matthew A. Howard, Department of Surgery (Division of Neurosurgery), University of Iowa College of Medicine, Iowa City, IA 52242. E-mail: mhoward@surgery.uiowa.edu

Received 11 February 1999; Revised 11 August 1999; Accepted 7 September 1999

agreement and understanding about the cytoarchitectonically distinct fields that together constitute 'belts' of auditory cortex surrounding AI, including fields on the lateral aspect of the STG.

Recently, Kaas and Hackett (1998) proposed a scheme of auditory cortical organization for New World and Old World monkeys based on available anatomic and electrophysiological evidence. According to this scheme, cortical processing of acoustic information may involve 15 or more interconnected cortical areas, grouped into four or more processing levels. Cortical fields at each level receive parallel thalamic input and interact serially with each other and with distant fields over corticocortical networks. Implicit in such a model is the concept that cortical fields outside the primary field(s) engage in higher-order complex processing, and results of single neuron studies in monkey are consistent with this hypothesis (Rauschecker et al., 1995; Rauschecker, 1998a,b). In the human, functional imaging (Petersen et al., 1988; Binder et al., 1994, 1996, 1997; Fiez et al., 1995, 1996; Griffiths et al., 1998) and direct electrophysiological recording (Ojemann and Engel, 1986; Creutzfeldt et al., 1987; Ojemann et al., 1988; Steinschneider et al., 1999) also suggest that these belt areas engage in complex sound processing in ways that are distinct from AI. Understanding the respective roles that each of these auditory areas plays in hearing, speech, and language requires gaining new knowledge about their locations, physiological boundaries, functional organizations and connections. To gain such information, we have begun to study human auditory cortex directly by using intracranial recording and electrical stimulation methods. The subjects were patients undergoing evaluation and surgical treatment of medically intractable epilepsy.

There is considerable intersubject and interhemispheric variability of temporal lobe gyral patterns (Geshwind and Levinsky, 1968; Galaburda and Sanides, 1980; Steinmetz et al., 1989; Penhune et al., 1996; Leonard et al., 1998) and their relationships to underlying cytoarchitecture, which have complicated efforts to understand the functional organization of human auditory cortical fields. Single-neuron mapping of auditory cortex in laboratory animals, including nonhuman primates, indicates clearly that the location, boundaries, and organization of auditory fields with respect to gyral patterns also vary considerably between subjects (e.g., Merzenich and Brugge, 1973; Merzenich et al., 1975). The earliest recording (Celesia et al., 1968; Celesia and Puletti, 1969, 1971; Puletti and Celesia, 1970; Celesia, 1976) and stimulation experiments (Penfield and Perot, 1963) performed on human auditory cortex were carried out acutely during surgery; thus, it was not feasible in any single subject to study electrophysiological or behavioral responses in detail or to map in any systematic way their spatial representations. These problems have now been partially circumvented by the introduction of two experimental approaches. The first is the ability to obtain in a single subject systematic data from many cortical sites with relatively high spatial resolution, thereby reducing localization errors that necessarily occur when data from mapping experiments are pooled across subjects (see also Liegeois-Chauvel et al., 1991, 1994; Boatman et al., 1994). The second is three-dimensional magnetic resonance imaging (MRI) (Damasio and Frank, 1992; Frank et al., 1997), which in our studies serves as an essential guide for electrode placement and for later alignment of cortical recording sites with anatomic landmarks.

The results presented in this study were derived from multicontact subdural recording arrays that were implanted over the lateral surface of the STG and, in a select subset of these patients, from multicontact modified depth electrodes (Howard et al., 1996b) inserted into HG. This chronic recording approach provided the opportunity to study over a period of several days in an individual subject the properties of acoustically evoked potentials, to map the spatial distribution(s) of the averaged EPs, and to compare the averaged EP waveforms recorded simultaneously from lateral STG and HG. In the course of these studies, EPs were recorded within a limited area on the lateral surface of posterior STG and in HG. EPs recorded simultaneously from STG and HG provided evidence that these areas represented the locations of two functionally separate fields. By stimulating HG electrically and recording from lateral STG sites, we obtained evidence that STG receives a short-latency input from HG. In addition, with a dense grid in place over the posterior lateral STG, we were able to show the spatial distribution of this corticocortical projection and its relationship to the EP map obtained with acoustic stimulation. Some of this work has been presented in abstract form (Howard et al., 1997, 1998).

MATERIALS AND METHODS

Human subjects

Research protocols were approved by the University of Iowa Human Subjects Review Board. Studies were carried out in patients undergoing surgical treatment for medically intractable epilepsy. Presurgical electroencephalography (EEG) and brain-imaging data provided essential information about the location of the seizure focus before surgical resection. Informed consent was obtained after the nature and possible consequences of the studies were explained to the patient. Patients did not incur additional risk by participating in these studies. All patients underwent preoperative WADA testing to determine hemispheric speech dominance. Results of pure tone audiometry carried out before the start of these studies all fell within the normal range.

Data presented in this study were derived from 13 patients in whom chronic electrodes were implanted for periods ranging from 2 to 17 days (median, 13 days). Scalp recorded EEG failed to adequately define the location of the seizure focus in these patients; thus, it was necessary for them to undergo a period of intracranial EEG monitoring and electrical-stimulation functional-mapping before resection surgery. The left hemisphere was studied in five of these patients and the right in eight. Five additional patients (three left, two right hemisphere) were studied in

Abbreviations

AI	primary auditory field
EEG	electroencephalography
EP	evoked potential
FTTS	first transverse temporal sulcus
HDE	hybrid depth electrode
HG	Heschl's gyrus
HS	Heschl's sulcus
MEG	magnetoencephalography
MRI	magnetic resonance imaging
PLST	posterior lateral superior temporal auditory area
STG	superior temporal gyrus
STS	superior temporal sulcus

the operating room during a 30-minute EEG recording session preceding surgical resection. Of the total, seventeen patients exhibited speech dominance in the left hemisphere and one (R11, Table 1) had bilateral speech representation.

Intracranial electrodes

A variety of electrodes were placed in cortical regions based on the clinical needs of the individual patient. With the dura mater reflected, and under direct visualization, one or more multicontact surface recording arrays (Radionics, Inc., Burlington, MA) were positioned to cover as much of the exposed surface of the lateral STG as possible. Frequently, electrode grids included parts of the adjacent parietal cortex and middle temporal gyrus. Surface recording arrays consisted of platinum-iridium disc electrodes embedded in a silicon membrane. The center-to-center spacing of the electrodes on a grid was 4 mm, 5 mm, 6 mm, or 1 cm. The diameter of the electrodes was 4.7 mm for the 1-cm spaced electrodes and 3.7 mm for the others. The contact exposure on the 4.7-mm electrode was 2.5 mm, whereas that on the 3.7-mm electrode was 1.6 mm. The number of electrodes in an array was either 20 (5×4), 60 (5×12), or 64 (8×8). Strip electrodes with 1-cm spacing were also used in some subjects.

In addition to the surface recording grids described above, modified depth electrodes (Hybrid Depth Electrode (HDE), Howard et al., 1996b) were stereotactically implanted into HG of the non–speech-dominant temporal lobe in five of the chronic patients. The HDE was oriented roughly parallel to the long axis of HG and was capable of recording electrical activity from as many as nine sites distributed over its length. Chronic recordings were obtained through grid and depth electrodes without compromising ongoing clinical EEG recordings. Intracranial recording and electrical-stimulation methods used in these studies were the same as those used routinely before or during epilepsy surgery to localize the focus of seizure onset and to identify functional areas of cortex. During recording sessions, the recording equipment and usually two or three experimenters were in the patient's room; patients were in a reclined position in a hospital bed. The room was kept as quiet as possible. Closed circuit television was also used to ensure that recordings were carried out while the patient appeared awake and alert.

Five patients in this study with unambiguous evidence of a unilateral, well-localized temporal lobe seizure focus underwent craniotomy and temporal lobe resection under local anesthesia without the aid of chronic subdural EEG recording. Limited EEG recording and electrical stimulation mapping were carried out during the craniotomy procedure to aid in determining the location and limits of the resection.

Anatomic imaging

A three-dimensional reconstruction was performed on the brain of each patient based on preoperative thin, contiguous MR images by using Brainvox (Damasio and Frank, 1992; Frank et al., 1997). The thickness of the MRI slices varied between 1.5 and 1.8 mm. The in-plane resolution was 0.9 mm for subjects studied early in the series, and 0.7 mm for later subjects. On the basis of these three-dimensional (3D) images HG was identified within the supratemporal plane. To provide information concerning the spatial relationship between HG (which cannot be visualized directly from the cortical surface) and PLST. Figure 1 illustrates a 3D MRI of a lateral surface (top) of a right cerebral hemisphere and of the superior temporal plane (middle) after overlying cortex was removed digitally to show the lateral projections of the posterior (P) and anterior (A) limits of the HG on the surface image of the STG. These landmarks are also shown in cross-sectional MRIs (bottom). The red line drawn on the image of superior temporal plane (middle) also shows the trajectory of a HDE. Postimplantation MRIs were also obtained. The acquisition parameters were the same for the pre- and post-implantation images. The final locations of the depth and surface electrodes were determined by using the 3D MRI technique described above, together with detailed photographs of the exposed surface of the brain taken during the implantation procedure. This information was used to construct EP maps of each subject, including those presented in this study.

In cases for which there were multiple HGs, the depth electrode always traversed the anterior of these, reaching its mesial portion where previous physiological and anatomic results indicate that AI resides. With a single multicontact electrode positioned within HG, it was not possible to obtain a comprehensive functional map of acoustically responsive regions throughout the gyrus or on surrounding areas on the superior temporal plane. Thus, we were unable to determine with certainty whether we recorded from field AI or from an adjoining auditory area. Although we tentatively conclude that our mesial depth recordings originated in area AI, we leave open the possibility that these recordings and those from more lateral recording sites were from acoustically active and cytoarchitectonically distinct fields that lie immediately adjacent to AI. Because of this uncertainty, we simply refer to our depth recording and stimulation as being within HG, which is interpreted to mean the mesial aspect of the anterior, or first, transverse temporal gyrus (Rademacher et al., 1993).

Acoustic stimulation and EP recordings

Brain potentials were amplified (Bak Electronics, Germantown, MD), filtered (bandpass 2–500Hz), digitized (1 kHz sampling rate, DataWave, Longmont, CO), displayed on-line, and stored for off-line analysis. An electrode on the ventral surface of the ipsilateral temporal lobe served as the reference electrode. The filter settings and reference electrode placement were selected for optimal recording of low frequency waveforms originating from superior temporal cortex. Typically, we recorded simultaneously from eight or 12 cortical sites and from each site averaged the results of 100 stimulus presentations. The acoustic stimulus was a train of acoustic transients consisting of five clicks with an interclick interval of 10 msec presented bilaterally by means of insert earphones (Etymotic Research, Elk Grove Village, IL). The click bursts were presented every 2 seconds with slight variation in the interstimulus interval to reduce contributions of synchronous noise to the averaged EP. A stimulus with these parameters was particularly effective in evoking relatively high amplitude stable potentials and, thus, was used routinely for locating and mapping the boundaries of acoustically responsive cortex. Sounds were delivered at a comfortable suprathreshold level for each patient, which was typically 50 dB above the detection threshold for the

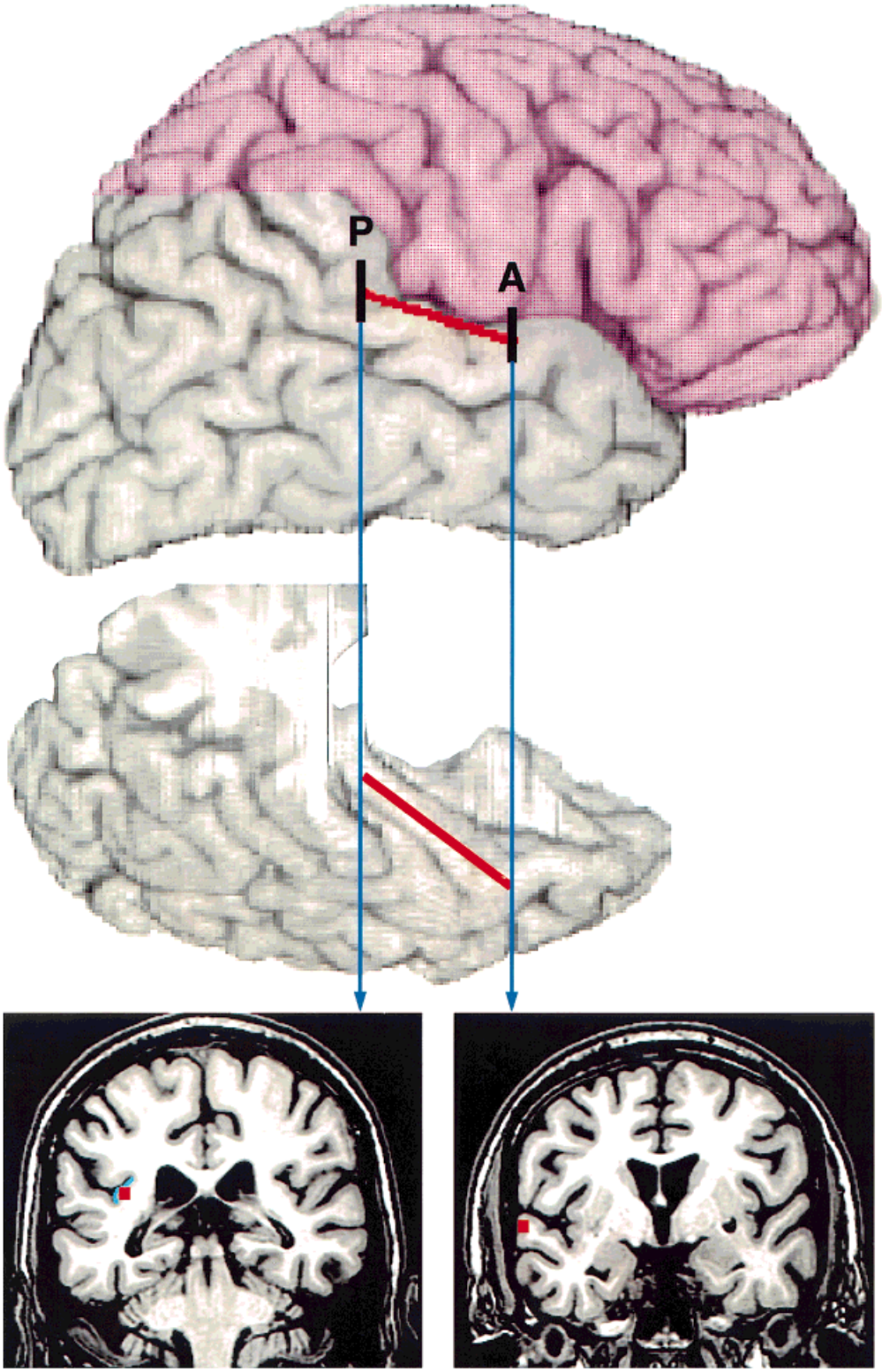

Fig. 1. Three-dimensional MRIs illustrating the method used to identify anatomic landmarks on the lateral surface of the cerebral hemisphere (top) and on the superior temporal plane (middle). The areas above the Sylvian fissure (shaded pink) were removed digitally and the remaining image rotated slightly to show the superior temporal plane. The red line on the superior temporal plane runs the length of Heschl's gyrus (see text for convention used to define transverse gyri). Blue lines show the posterior (P) and anterior (A) boundaries of HG projected onto the lateral surface. Black vertical bars mark these boundaries here and on all MRIs associated with evoked potential maps. Coronal MRIs (bottom) were obtained at the anterior and posterior margins of HG (see text for parameters). Red dots mark endpoints of the red line shown in the middle panel, indicating the medial and lateral limits of HG. See also Figure 11 legend for orientation to anatomic landmarks. For abbreviations, see list.

click train stimulus. Threshold was estimated against the background sounds in the patient's hospital room. For each stimulus presentation, 1 second of the waveform was digitized and a running average computed and displayed on-line.

Electrical stimulation

Constant-current bipolar electrical stimulation was applied to adjacent grid or depth electrode sites by a Grass SD9 stimulator (Astromed-Grass, Providence, RI) or a computer-controlled stimulus generator custom built by the University of Iowa Department of Biomedical Engineering. Current strengths were maintained below afterdischarge threshold (Ojemann and Engel, 1986). Two stimulus paradigms were used, both by using charge-balanced square waves (0.2-msec duration). The aim of using the first paradigm was to identify by standard electrical-stimulation functional-mapping methods (Ojemann and Engel, 1986) those loci where stimulation evoked or altered an acoustic sensation or disrupted speech function. Here, the stimuli were pulse trains delivered at a frequency of 50 Hz and current strengths of 4–10 mA. This clinical mapping technique is used widely by epilepsy surgeons to localize cortical regions that subserve speech, motor, and somatosensory functions to avoid damaging these sites during the resection procedure. The aim of using the second stimulus paradigm was to activate a localized area of cortex while recording from other cortical sites, thereby studying possible functional connections between cortical fields. In the present study, we focused on the possible functional connection between HG and the lateral surface of the STG. This experiment was carried out by delivering single electrical pulses to HG (1 or 2/second, 1–4 mA), while recording simultaneously from the electrode grid on the lateral STG. Thus, the spatial distribution of averaged EPs obtained by electrical stimulation was compared directly with the EP map obtained from the same grid with acoustical stimulation in the same subject. In addition, sites on STG were stimulated and recordings were made from the depth electrode in HG. In both experiments, the averaged waveform from 100 stimulus trials was computed and displayed on-line, as described above for acoustic stimulation. Electrical stimulation with these parameters is not perceived by the subject. It is a safe procedure that has been used previously to study functional connections between temporal lobe regions in neurosurgical patients (Wilson et al., 1990).

RESULTS

Features of the averaged evoked potential

In each of 13 patients with chronically implanted electrode arrays, click trains elicited EPs from only a limited area along the lateral surface of the posterior STG (Figs. 5, 6, 7, 9, 10). We refer to this area on the STG as the posterior lateral superior temporal field, or PLST (see Discussion section). Typically, there was one electrode site at which the peak-to-peak amplitude of the EP was maximal; the amplitude of the EP decreased more or less abruptly around this site (Figs. 5, 10). In five cases, there was evidence for a second focus of EP activity (Figs. 6, 9), and in one case a possible third (Fig. 7).

Figure 2 illustrates five superimposed averaged EPs recorded under the same stimulus conditions from the same STG site on five successive occasions over a period of 6 days. The EPs show both the time structure of the waveform and its variability over days of recording. The EP was characterized by an initial positive peak (P_α) followed by a negative component (N_α) and then by additional positive (P_β) and negative waves (N_β) of smaller amplitude. We use this notation for the waveform peaks to distinguish between auditory EPs recorded directly from the brain and those recorded from the scalp by others (see Kraus and McGee, 1992). Table 1 lists for each subject in this study the latencies of major peaks in the EP recorded at the site of maximal response. As can be seen from these latency measurements as well as from the waveforms on the EP maps, the major components of the averaged EP illustrated in Figure 2 were identified across subjects, although the latency and relative amplitudes of the peaks could vary across electrode sites in any one subject and among subjects. Because of surgical time constraints, long-term response variability in the EP could not be studied in intraoperative cases.

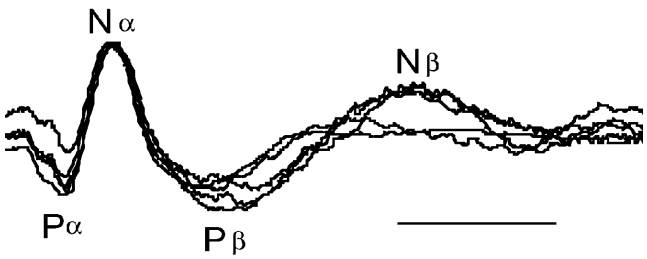

Fig. 2. Five superimposed evoked potentials recorded from a single site on lateral STG in patient R32 during five different recording sessions over a 6-day period. EPs shown were derived from recordings at the focus of maximal response on the posterior STG to click trains presented bilaterally at a moderate sound intensity. Waveforms are labeled to indicate the polarity (N, negative; P, positive) and temporal sequence of the peaks. Greek subscripts identify EP waveforms and differentiate them from EPs obtained with scalp recording (see Kraus and McGee, 1992). For abbreviations, see list. Time = 100 msec.

TABLE 1. Posterior Lateral Superior Temporal Auditory Area Peak Latency

	Peak latency (msec)			
Subject	P_α	N_α	P_β	N_β
Chronic				
R11	52	104	197	374
L15	63	117	182	274
R16[1]	44	80	146	276
L18	36	90	150	300
L21	40	84	128	212
R25[1]	36	73	142	237
R32[1]	34	67	123	255
L37	48	81	120	282
L40	40	117	182	250
R42	41	68	135	184
R43[1]	48	98	163	291
R44	40	100	253	358
R48[1]	51	106	169	269
Intraoperative				
R20	39	84	151	210
L24	69	102	193	310
L26	40	58	117	193
R27	50	91	200	300
L28	44	106	168	296
Mean	45.3	90.3	162.2	270.6
STD	9.3	17.2	35.1	51.6
Median	42.5	90.5	157.0	275.0
Range	34–69	58–117	117–251	184–374

[1]also HG depth electrode.

The averaged EPs recorded from HG depth electrodes were similar in shape across recording sites in the same subject but, unlike those recorded in STG, could differ markedly between subjects, as can be seen by comparing the waveforms in Figure 3a,c. We attribute this intersubject difference in HG waveform to the likelihood that across subjects the recordings were made in different cortical layers. Earlier studies noted similar intersubject differences in the polarity of the polyphasic waveforms recorded from HG, which were attributed to the recording electrode being placed on different sides of the generating dipole (Celesia and Puletti, 1969; Liegeois-Chauvel et al., 1991; see also Steinschneider et al., 1992). Although our postimplantation MRIs revealed clearly each of the electrode contacts within the cortical gray matter, this method did not provide sufficient resolution to determine the laminar distribution of recording sites.

We sought further evidence that EPs recorded in HG and STG were derived from different fields of auditory cortex. We obtained simultaneous recordings from sites on both HG and STG while acoustic stimuli with different interstimulus intervals were presented (Fig. 3). The HG recordings were from the mesial electrode sites, presumably in primary auditory cortex. The PLST recordings were from the sites at or near where EP amplitude was greatest in response to click-train stimulation. PLST recovery functions tended to be similar to each other but, at short interstimulus intervals, were clearly separable from those derived from HG recordings. In both subjects, at the shortest interstimulus intervals, there was a marked difference in the amplitudes of the EPs at the HG and PLST sites. As interstimulus interval lengthened, the amplitudes of the EPs at the two sites increased, converging at the control interstimulus interval of 2 seconds. We also were able to study in three cases the EPs recorded simultaneously at both the HG and STG sites before and just after induction of general anesthesia. Figure 4 illustrates the general finding that the entire EP recorded in PLST was abolished within approximately 3 minutes of induction of general anesthesia. In HG, only the later components of the EP were reduced or abolished, leaving the early negative component attenuated in amplitude but otherwise largely intact.

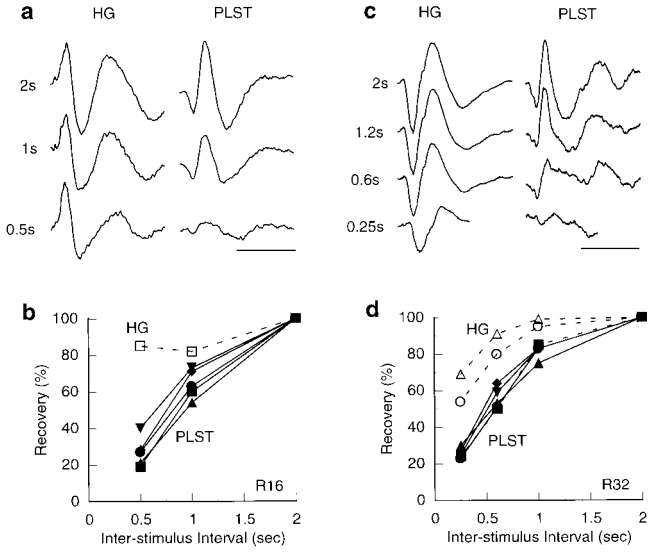

Fig. 3. **a,c:** Averaged EPs recorded simultaneously in HG and STG in two chronically implanted subjects when the interval between the click trains was changed. Time = 200 msec. **b,d:** Recovery functions, plotting the change in amplitude of N_α of the EP recorded from STG and that recorded from HG. Data are normalized to the response recorded with an interstimulus interval of 2 seconds. For abbreviations, see list.

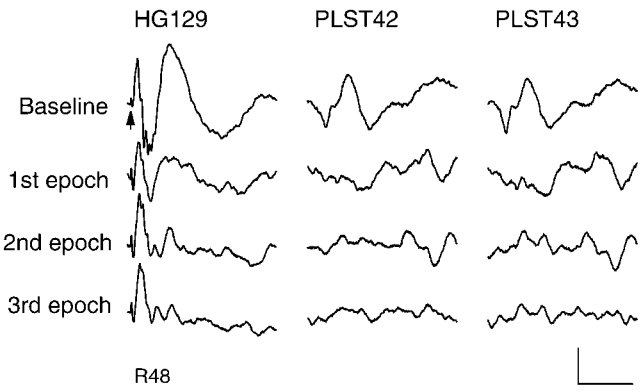

Fig. 4. EPs recorded simultaneously from foci of maximal response in HG and PLST before (Baseline) and during three epochs after induction of general anesthesia. Anesthetic: thiopental (250-mg bolus) and remifentanyl (25 μg/min per kg). Average of 100 repetitions of click trains repeated one every 2 seconds. Thus, each EP represents 200 seconds of recording. The interval between recording epochs was about 30 seconds. By the third epoch the patient was under deep anesthesia. For abbreviations, see list. Time = 200 msec, amplitude = 40 μV (HG) or 80 μV (PLST).

Distribution of STG averaged evoked potentials

The distribution of averaged EPs was plotted for each patient. These results were then aligned with the sulcal landmarks aided by 3D MRI reconstructions (e.g., Fig. 1) and intraoperative photographs. The five EP maps presented in this study illustrate that some map features were consistent across subjects and that other features varied. Figure 5 illustrates a map obtained from the left (dominant) hemisphere of one subject; maps shown in Figures 6, 7, 9, and 10 were obtained from the right (nondominant) hemispheres of four additional subjects. The position of the electrode array(s) varied from one subject to the next but usually included most of the posterior portion of the STG (shown by the shaded area on the MRIs) and often a segment of the middle temporal gyrus ventrally and parietal cortex dorsally.

In all 18 cases, there was at least one area on the posterior STG where the amplitude of the auditory EP was greatest, with EP amplitude falling off with distance from that focus of maximum amplitude. Figures 5 and 10 illustrate cases for which a single prominent EP focus of activity was found within the boundary of the grid. In other subjects, there were clearly two areas of EP activity, which were separated by a region in which there was little or no auditory-evoked activity in evidence (Figs. 6, 9). In one case, a possible third focus of activity was observed (Fig. 7). The sizes of the areas in which EPs were recorded varied from subject to subject, with the maps in Figures 7c and 9c showing the two extremes. In some (e.g., Fig. 7), we may have only recorded from a portion of a posterior EP focus because it fell close to the grid border. From examina-

tion of all the maps obtained with click-train stimulation, we estimate that an acoustically responsive zone could extend up to several centimeters rostrocaudally and dorsoventrally on the posterior STG. It also seemed clear that the areas of highest amplitude EP were located dorsally on the STG and in some cases quite close to the crown of the gyrus. In several cases (e.g., Figs. 7, 10), EPs on posterior STG were recorded from electrodes that appeared to make contact with the dorsal lip of the lateral fissure, although it is more likely that they were over the pia mater that spans the fissure. We interpret these EPs as arising from the ventral lip of the lateral fissure on the STG. There was also

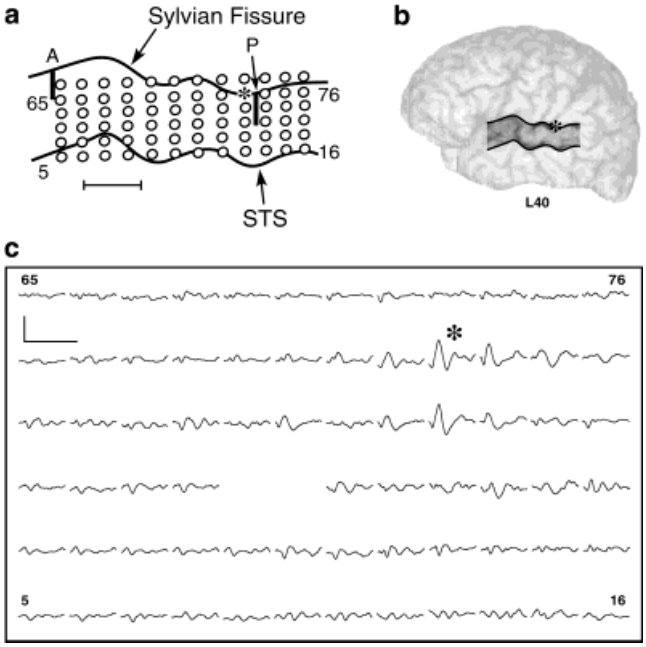

Fig. 5. Distribution of averaged auditory EPs on the lateral surface of the left STG in one subject (L40). **a:** Diagram showing the subdural electrode array in relationship to the Sylvian fissure, superior temporal sulcus (STS), and the lateral projections of the anterior (A) and posterior (P) boundaries of HG. The numbers at the corners identify the ends of rows of numbered contacts on the electrode array and provide references to the EPs recorded from each of these contacts, as shown in c. **b:** MR image of the lateral surface of the right cerebral hemisphere with the area of STG beneath and adjacent to the electrode grid highlighted. **c:** Spatial distribution of auditory EPs recorded from the grid shown in a. EP map was created from the average of 100 responses to binaural presentation of a 100 Hz click train repeated one every 2 seconds. Asterisk identifies the focus (or foci) of high-amplitude averaged EP. For abbreviations, see list. Distance = 1 cm, time = 400 msec.

a relatively consistent spatial relationship between the area of EPs on the STG and the lateral boundaries of HG and planum temporale. Figure 11 illustrates the estimated location and extent of PLST.

The extent to which the waveform of the EPs or the boundaries of the auditory responsive area on STG might change with changes in stimulus parameters is not known. Changing stimulus intensity can alter the latencies and amplitudes of the EP peaks and valleys. Evoked responses to tone bursts and noise bursts were recorded in the same area from which we recorded click-evoked potentials, but we did not obtain sufficient data to determine their full

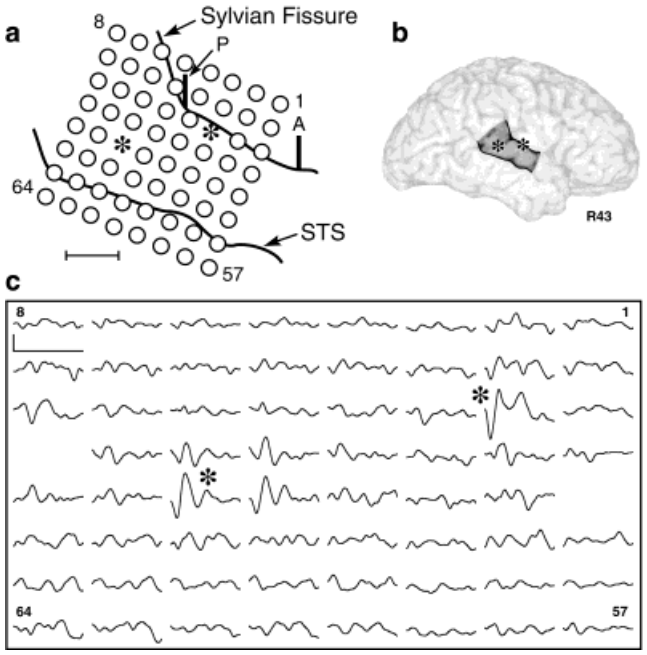

Fig. 6. **a–c:** Distribution of averaged EPs evoked by click trains on lateral surface of the right STG of one subject (R43). See Figure 5 legend for details. For abbreviations, see list.

extent or the degree of overlap. Although electrode grids were often placed all along the STG, clear EPs to click trains were not elicited from the anterior portion of the gyrus. EPs were often recorded on the parietal cortex (postcentral and supramarginal gyri) at sites distant from the EP areas on the STG, as shown by the recordings from the most dorsal row of electrode sites in Figure 7. We also recorded EPs from electrodes on the inferior frontal gyrus.

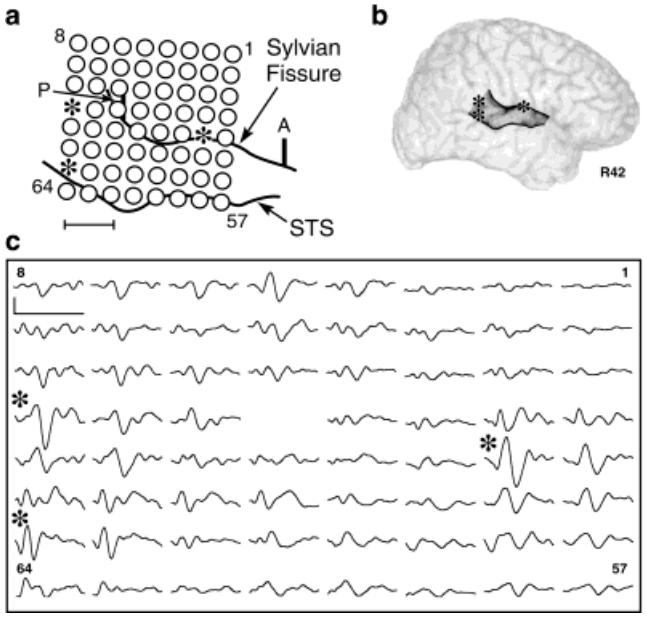

Fig. 7. **a–c:** Distribution of averaged EPs evoked by click trains on lateral surface of the right STG of one subject (R42). See Figure 5 legend for details. For abbreviations, see list.

We have no evidence for auditory-evoked activity on the middle temporal gyrus. The details of recordings beyond the temporal lobe are outside the scope of this study. Although EP maps were recorded from posterior STG of both the left (dominant) and right (nondominant) hemispheres, we did not record from the left and right hemispheres in the same subject and our sample size is not adequate to determine the extent to which there may be systematic differences in EP maps or EP waveforms related to laterality of recording.

Evidence for a connection between HG and STG

We stimulated the HG site from which the highest amplitude auditory EP was obtained while recording from STG sites previously mapped by auditory stimulation (Fig. 8). The locations of the bipolar pairs of stimulating electrodes in HG and the sites of recording of the EPs are shown in the insets of Figures 9 and 10. The EPs exhibited an initial surface-positive peak for electrical stimuli just above threshold; as stimulus strength was raised, the EP

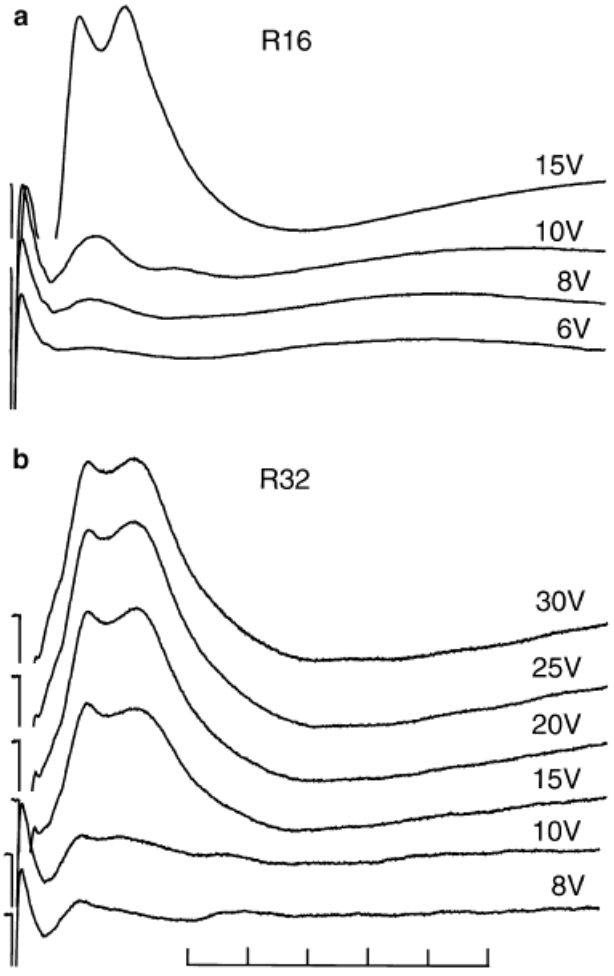

Fig. 8. Averaged EPs recorded at the site of maximal response in right STG in response to electrical stimulation of HG for the two subjects (R16 and R32) illustrated in Figures 9 and 10. EPs are seen growing and changing configuration as the strength of the electrical stimulus is increased from its near-threshold voltage. For abbreviations, see list. Time bar = 50 msec.

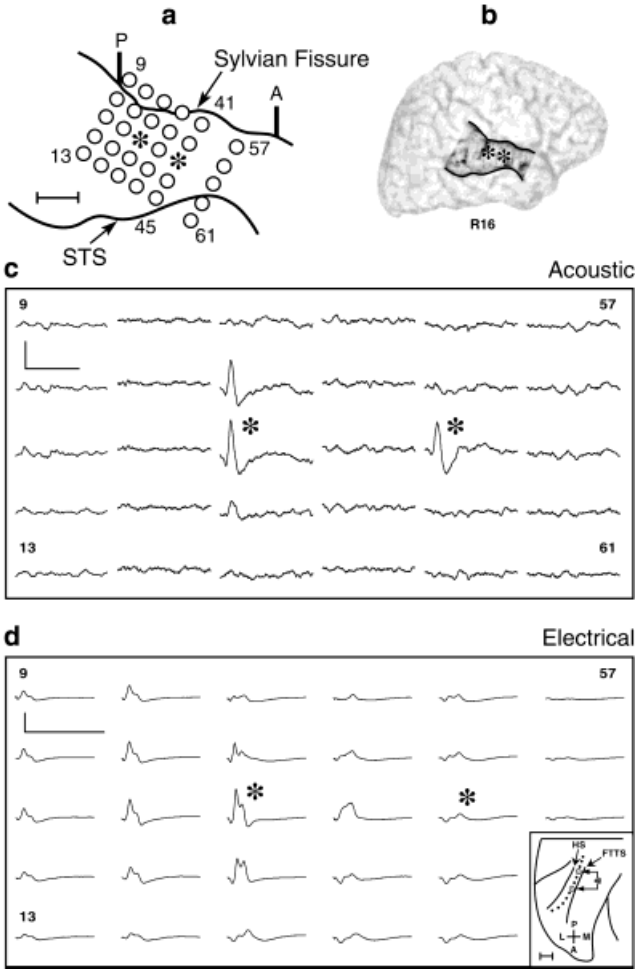

Fig. 9. **a–d:** Distribution of averaged EPs to click trains (c) and to electrical stimulation of HG (d) on lateral surface of the right STG of one subject (R16). See Figure 5 legend for details of the orientation of the grid and the acoustic EP map. The spatial distribution of EPs resulting from bipolar stimulation of adjacent HG sites shown in d. The layout of the recording sites in c and d are the same to facilitate comparisons. **Inset:** drawing of superior temporal plane and the location of the depth recording sites, derived from MRI data. HS, Heschl's sulcus; FTTS, first transverse temporal sulcus. For abbreviations, see list.

became biphasic with a prominent dual-peak negative component emerging at higher stimulus levels. The peaks were about 10 msec apart. Onset latency was selected as the time at which the waveform first demonstrated a clear deflection from baseline. The shortest onset latencies measured ranged from 2.5 to 3.0 msec. Earlier components, if they existed, would have been obscured by the stimulus artifact.

Figures 9 and 10 illustrate for two subjects the spatial distribution of averaged EPs on the STG elicited by electrical stimulation and its relationship to the spatial distribution of averaged EPs evoked by click trains. In the acoustic EP map of Figure 9c, two EP foci were found, whereas the map shown in Figure 10c exhibits a single focus of activity. Figures 9d and 10d show that the distribution of EPs on the STG resulting from electrical stimulation of HG overlapped the map of auditory EPs

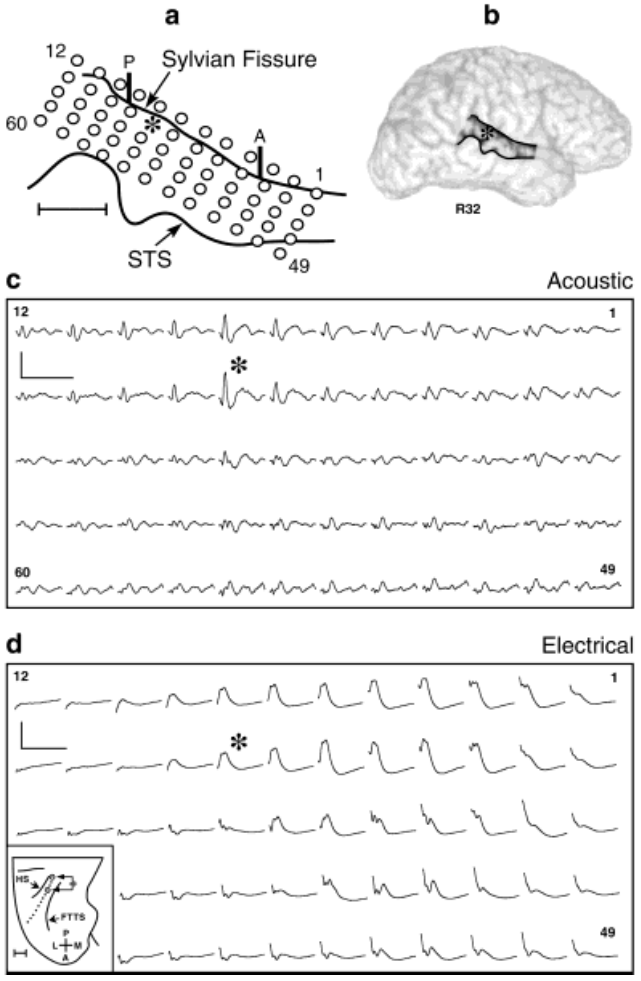

Fig. 10. **a–d:** Distribution of averaged EPs to click trains (c) and to electrical stimulation of HG (d) on lateral surface of the right STG of one subject (R32). See Figures 5 and 9 legends for details. For abbreviations, see list.

obtained in the same subjects. In subject R16 (Fig. 9), the EPs having the maximal amplitude to electrical or acoustic stimulation were recorded at the same STG electrode site (asterisks), although the EP map obtained by HG electrical stimulation was more extensive than that obtained by acoustic stimulation. The map obtained in patient R32 (Fig. 10) by using electrical stimulation was also extensive, with the largest EP occurring near the site of the maximal response to acoustic stimulation. However, in this case, the stimulus artifact obscured some of the details of the EP waveform, especially along the three most rostral rows of electrodes. Preliminary analysis of data obtained while stimulating acoustically active sites within PLST and recording from HG suggests the existence of reciprocal connections between these two fields. Studies of the possible functional relationships between STG and HG are ongoing.

Sensations evoked by electrical stimulation of STG

During the course of clinical electrical stimulation mapping, a number of auditory sensations were evoked that were similar to those reported by Penfield (Penfield and Perot, 1963). Electrically stimulating the site of maximal EP evoked by clicks in PLST elicited in all chronic patients either auditory percepts (e.g., "swooshing of jumping rope," "whining," "jet engine," etc), or an alteration in the perception of sound in their environment (Fig. 11). No patients reported hearing human speech, voices, or music. In left hemisphere cases, electrical stimulation of the STG focus of maximal response did not disrupt patients' abilities to count, name objects, follow verbal commands, or generate meaningful spontaneous speech, although disruption of naming was noted at other left posterior temporal lobe sites.

DISCUSSION

We have shown in the awake human subject that click trains of moderate intensity evoke a prominent polyphasic response that is confined to a limited area of the posterolateral superior temporal gyrus and is stable over days of recording. Based on sensitivity to stimulus rate and general anesthesia, the averaged EP recorded in STG can be differentiated from the averaged EP recorded simultaneously from HG, the presumed site of the primary auditory field. The acoustically active STG area is represented on both the left (dominant) and right cerebral hemispheres. We have no evidence that the EPs recorded on the lateral STG are the result of evoked activity volume conducted from HG (see Lee et al., 1984). Hence, we tentatively consider the area on the posterior aspect of STG that responded to click trains a single auditory area, which we refer to as the *posterior lateral superior temporal* auditory area (PLST).

The peak latencies of the averaged EP waveform were all within the range of those of the middle latency and late auditory or event-related potentials identified in magnetoencephalography (MEG) (Hari, 1990; Pantev et al., 1995) and EEG (Kraus and McGee, 1992; Pantev et al., 1995) recordings (see also Goff, 1978). Although our experiments were aimed primarily at auditory areas on the lateral STG, we also recorded from a limited number of sites in HG of five subjects. HG evoked potentials were characterized by a series of waves, beginning with a small short-latency peak. The polarity of the HG waves could differ across subjects, presumably because of the location of the recording site with respect to the source dipole. These observations are in general agreement with others who have recorded in this area (Celesia et al., 1968; Celesia and Puletti, 1969, 1971; Puletti and Celesia, 1970; Celesia, 1976; Lee et al., 1984; Liegeois-Chavel et al., 1991, 1994).

Induction of general anesthesia had a differential effect on the HG and PLST response. The early components of the EP recorded in HG of the awake subject were reduced in amplitude but clearly recognizable under anesthesia (see also Lee et al., 1984), whereas later components were severely attenuated or eliminated. Celesia and Puletti (1971) observed similar differences between HG evoked potentials recorded in awake patients and EPs recorded from the same area in a different population of patients under general anesthesia. Results similar to these were also obtained by Kral et al. (1999) from area AI of the cat. In contrast to the HG evoked potentials, we found that the PLST responses were eliminated by general anesthesia, in agreement with observations of Celesia and Puletti (1971). These results are also consistent with earlier data of

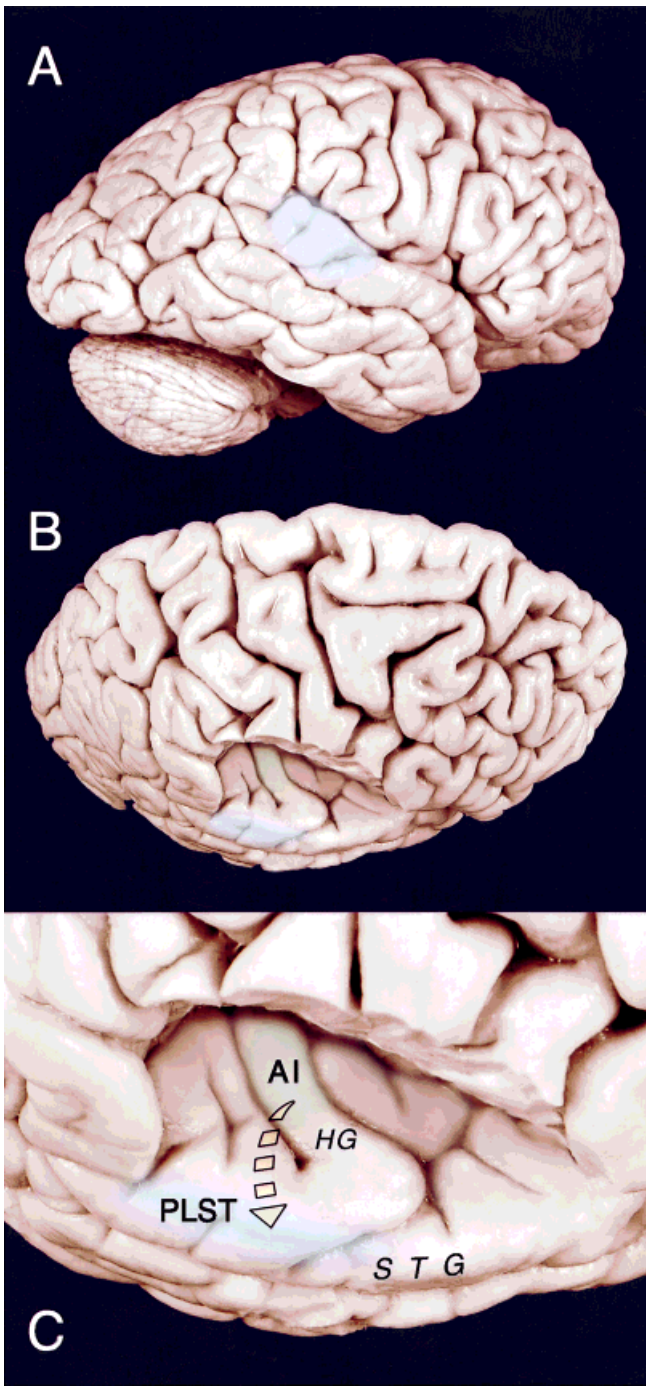

Fig. 11. Photographs of the lateral surface (**A**) and superior temporal plane (**B,C**) of a postmortem human brain showing the relative size and location of PLST (blue) estimated from the distributions of averaged click-evoked EPs recorded in our experimental subjects. The mesial auditory field on HG from which auditory EPs were recorded is designated AI (green). The dashed arrow indicates a projection from the mesial HG auditory field (AI) to PLST. For abbreviations, see list.

Woolsey (1971) showing the click response map in the anesthetized chimpanzee confined to the superior temporal plane. They also agree with the findings in the monkey that under general anesthesia responsiveness of lateral superior temporal gyrus to clicks and tones is relatively poor compared with that of the primary field (Pribram et al., 1954; Merzenich and Brugge, 1973; Rauschecker et al., 1995; Rauschecker, 1998a). General anesthesia has also been shown to eliminate preferentially the middle latency components of auditory-evoked potentials recorded from the scalp of awake humans (Madler et al., 1991), again pointing at PLST as one source of these waves. Libet et al. (1967) and Ray et al. (1999) have shown that, although the presence alone of an early EP in primary somatosensory cortex evoked by a peripheral stimulus is a necessary event for conscious awareness of the stimulus, it is not sufficient; later waves, lasting several hundred milliseconds must also be present. If the same situation obtains in auditory cortex then it would appear that general anesthesia preferentially attenuates or eliminates those later waves associated with conscious awareness of a sound.

The systematic differences in the time course of recovery of EPs, derived from recordings made simultaneously in HG and lateral STG sites, provided additional evidence that these were two separate fields. As interstimulus intervals shortened, the amplitude of EPs recorded from PLST decreased to a much greater degree than EPs recorded from HG. The pattern of rate sensitivity we observed from our HG recordings was consistent with previous reports of direct recordings from HG in humans (Puletti and Celesia, 1970, Celesia 1976, Liegeois-Chauvel et al., 1991) and from AI in experimental animals (see Litovsky et al., 1999).

Lee and colleagues (1984) recorded low amplitude short latency EPs from peri-Sylvian cortex by using a continuous train of clicks at 6.8 Hz (147-msec interclick interval). Our results indicate that such a stimulus would evoke from PLST either a very weak response or no response at all. The EPs they recorded from STG resembled those previously recorded directly from HG, were maintained under general anesthesia, and exhibited a frequency after response at a click rate of 40 Hz. These findings led the authors to conclude that responses they recorded on the STG represented EPs that were volume-conducted from HG. Although it is likely Lee et al. reached the correct conclusions from their results, our findings of clear differences in sensitivity of HG and lateral STG to general anesthesia and to changes in rate of stimulation led us to conclude that we were recording from different cortical fields.

Differences in the EP responses recorded from HG and PLST may result in part from differences in thalamic input to the two fields. If thalamocortical projections in the human forebrain are comparable to those in monkey (reviewed by Kaas and Hackett, 1998) then human A1 would receive its main thalamic input from the ventral division of the medial geniculate body. In contrast, fields on the lateral aspect of the STG would receive their projections mainly from the dorsal and medial divisions of MGB and from the suprageniculate/limitans and medial pulvinar nuclei. Following this line of reasoning, the mesial recording sites in HG would then occupy a portion of the "auditory core" and PLST a portion of the "auditory parabelt." Our finding that PLST exhibits longer time constants than HG, and the fact that this area, in addition to having different thalamic inputs, receives projections from the primary field on HG, would suggest that PLST is engaged in further processing of these sound sequences having very long temporal intervals (see also Phillips and Farmer, 1990; Griffiths et al., 1998).

We were able to obtain relatively detailed maps of the distributions of averaged EPs in single subjects with grid electrodes covering much of the posterior lateral STG. Celesia and his colleagues, after extensive recording in many subjects, reported two areas of acoustic-evoked potentials: one on the supratemporal plane and another more extensive region around the Sylvian fissure on the lateral surface of the STG and the parietal lobe (summarized by Celesia, 1976). Without the benefit of modern recording grid arrays and brain imaging methods, they were unable to map systematically in a single subject the spatial extent of acoustically sensitive STG and to relate accurately the electrophysiological results to anatomic landmarks on the lateral surface of the STG and on the superior temporal plane. Moreover, without simultaneous recordings from HG and surrounding STG cortex, it would have been difficult to determine with certainty whether the recorded EPs were from the same or different fields. Our data show considerable intersubject variability in the distribution of EPs with respect to fissural patterns on the lateral STG. Similar differences in auditory maps across subjects have been recognized in animal experiments (e.g., Merzenich and Brugge, 1973; Merzenich et al., 1975). Indeed it may have been the pooling of data across many subjects that accounts for the relatively broad acoustically active region illustrated by Celesia (1976) on and around the STG.

Amplitude gradients of PLST-evoked potentials, some quite steep, were observed on the lateral STG around a region (or regions) of high EP amplitude, providing additional evidence that the neural sources for the response were located within the region of the gyrus directly beneath the recording contacts or in very close proximity to them. We have not mapped in detail the supratemporal plane and, therefore, must leave unanswered the question of whether and to what extent field PLST extends on to the superior surface of the STG. Liegeois-Chauvel et al. (1991, 1994) recorded auditory EPs by using multiple cylindrical penetrating depth electrodes stereotactically implanted along lateral-medial trajectories such that simultaneous recordings could be obtained from presumed A1 cortex (mesial HG) and immediately adjacent acoustically sensitive cortex (planum temporale and lateral HG) on the supratemporal plane. All of their patients were awake and studied outside the operating room. Although comparison between their results and ours is made difficult because of differences in acoustical stimuli and recording conditions, based on the latency of peaks and valleys in the EP, it would appear that the first positive deflection we recorded in PLST, with a peak latency between about 35 and 70 msec, spans the P50 peak they recorded from the lateral extension of HG or the planum temporale, whereas the second, negative, deflection is within the range of the N75 and N120 potentials (Liegeois-Chauvel et al., 1994). Our preliminary results from depth recordings indicate that EPs recorded in lateral HG may differ from those in mesial HG. From earlier work (Liegeois-Chauvel et al., 1994), it appears that there may be at least one other auditory field situated between PLST and HG, which would be consistent with the cytoarchitectonic parcellation of this part of the human temporal lobe. Results of MEG recordings indicate that activation of cortex in this region contributes to the 100 msec latency (N1m) component of the auditory-evoked response (Lütkenhöner and Steinsträter, 1998). Again extrapolating from data obtained in the monkey (Kaas and Hackett, 1998), we might consider this region part of the "auditory belt," lying between mesial HG ("auditory core") and PLST ("auditory parabelt").

The observation that in some cases there were multiple foci of evoked activity suggests that area PLST may be subdivided or that it may represent more than one distinct cortical area. Given the localized nature of EP foci often found within PLST, it may also be possible that additional foci were overlooked when grids with comparatively large intercontact distances were used early in the series. PLST appears to correspond to a portion of Brodmann's area 22. However, in the human, area 22 is not homogeneous in its cytoarchitecture and, thus, PLST may overlap substantially with several of the cytoarchitectonic subdivisions of the STG described by later anatomists (Economo, 1929; Hopf, 1964; Galaburda and Sanides, 1980). In our human studies, it is not possible to correlate directly the boundaries of physiological maps with the underlying cytoarchitecture. However, in the monkey the boundaries of multiple auditory fields on the superior temporal gyrus defined electrophysiologically (Merzenich and Brugge, 1973; Imig et al., 1977; Morel and Kaas, 1992; Morel et al., 1993; Rauschecker et al., 1995; Rauschecker, 1998a,b) correlate well with the boundaries defined by the underlying cytoarchitecture (Burton and Jones, 1976; Pandya and Sanides, 1973; Hackett et al., 1998). Thus, our conclusion that PLST is a single auditory area remains tentative until further studies are carried out. Such studies will include a wider range of acoustic stimuli, including speech sounds and greater attention to the behavioral state of the subject.

While applying electrical stimulation to sites in HG, we recorded short-latency evoked responses in PLST. The stimuli were single short electrical pulses that did not evoke auditory sensations. This result suggests the existence of a projection of HG upon PLST. Early neurophysiological studies of the temporal auditory fields in the chimpanzee (Bailey et al., 1943) and rhesus monkey (Ward et al., 1946; Sugar et al., 1948) showed that when strychnine was applied to primary auditory cortex, spikes were profusely propagated into area 22. Later electrophysiological (Bignall, 1969) and anatomic (Kaas and Hackett, 1998; Hackett et al., 1998) results have confirmed and elaborated upon these and other auditory corticocortical connections in the nonhuman primate. Liegeois-Chauvel et al. (1991) applied single shocks to the dorsoposterior region of HG in a human patient and elicited evoked responses with a 6–8-msec latency on the lateral aspect of HG itself, suggesting a polysynaptic corticocortical projection to this area. In our studies, short latency potentials were observed over a region of lateral STG that overlapped PLST, thus revealing for the first time in the human a functional connection between these two auditory fields. We were unable to ascertain whether this is a direct connection between the two areas or an indirect one, the latter being consistent with the hierarchical connectivity model of Kaas and Hackett (1998) based on extensive electrophysiological mapping and neuroanatomic tracer studies in the monkey. The EP elicited by electrical stimulation had an onset latency in the order of several milliseconds and, at the highest stimulus levels used, exhibited dual negative peaks, which suggests that the PLST was activated over a polysynaptic pathway from HG. That such a connection can be demonstrated between HG and PLST also lends further credence to our interpretation of PLST being a field distinct from HG. Griffiths et al. (1998) have suggested

that such circuitry may be involved in emergent temporal properties of cortical processing.

When pulse trains of electrical stimuli were delivered at the focus of maximal response within PLST, the subjects reported hearing sounds or experiencing a change in their perception of ambient sounds. The nature of these perceptions was similar to the auditory responses or crude auditory sensations described by 16% of Penfield's patients after electrical stimulation of the lateral STG or HG (Penfield and Jasper, 1954). Evoked percepts were always reported as being heard at the contralateral ear. Sites in the language-dominant hemisphere evoking auditory perceptions did not colocalize with sites causing speech arrest; findings that are consistent with those of Penfield. None of our patients described auditory "experiential" responses or hallucinations of things previously heard, as Penfield observed in 2.1% of his patients after electrical stimulation of the lateral STG (Penfield and Perot, 1963). Current evidence would suggest that experiential responses do not occur after electrical stimulation of cortex unless activity is propagated to limbic structures (Gloor et al., 1982). In our series, techniques were available, and care was taken, not to induce after-discharges that could result in propagation of epileptiform activity to mesial structures.

Whereas direct stimulation of PLST sites with a 50 Hz train of electrical pulses resulted in conscious perception of sound, activation of these same sites by a single electrical pulse, either directly or indirectly by means of a corticocortical projection from HG, failed to do so. These observations are consistent with the results of direct electrical stimulation of somatic sensory (Libet et al., 1964; Ray et al., 1999) or visual cortex (Ray et al., 1999), namely that a relatively long "utilization train duration or utilization time" (Libet et al., 1964) is necessary to produce a sensory experience.

There is growing evidence from modern functional brain imaging studies in humans (Petersen et al., 1988; Binder et al., 1994, 1997; Fiez et al., 1995) that the STG may be made up of multiple functional areas, each engaged in different aspects of complex acoustic processing. Increases in cerebral blood flow associated with perceptual analysis of speech (Petersen et al., 1988; Binder, 1995; Fiez et al., 1995, 1996; Price et al., 1996; Zatorre et al., 1996a; Binder et al., 1997) with melodic patterns (Griffiths et al., 1998), or with acoustic imagery (Zatorre et al., 1996b), have been reported in an area that appears to overlap field PLST. Electrophysiological recordings in the rhesus monkey (Rauschecker et al., 1995; Rauschecker, 1998a,b) and in the human (Ojemann and Engel, 1986; Creutzfeldt et al., 1987; Ojemann et al., 1988; Steinschneider et al., 1999) are in general accord with the human functional imaging findings that the lateral STG is involved in processing complex acoustic signals, including speech. The data presented in this study were obtained by using click-train stimulation. This approach was a necessary first step in identifying and mapping the extent of acoustic cortex in the lateral temporal lobe in human. Further studies that use more complex signals, including speech sounds, are presently under way. Furthermore, although averaged acoustic-evoked potentials reveal the presence of acoustic input to the cortex, they fail to show the moment-by-moment changes in excitability that may occur in naive awake subjects. Despite these limitations, the data presented provide direct evidence of an auditory association cortical area on STG and add to our emerging understanding of an organizational framework for human auditory cortex, which is a necessary step for discerning its functional role(s) in hearing and speech perception.

ACKNOWLEDGMENTS

We thank all of our patients who generously agreed to participate in these studies. They gave unselfishly of their time and effort to help advance scientific knowledge. We also thank Carol Dizack for her help with computer graphics. M.H. received support from The Hoover Fund and the Carver Trust. M.S. received support from the Beth Abraham Hospital Institute for Music and Neurological Function. M.H., M.S., and J.B. were supported by NIH grants.

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