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Automatic and Intrinsic Auditory "What" and "Where" Processing in Humans Revealed by Electrical Neuroimaging

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The auditory system includes 2 parallel functional pathways—one for treating sounds' identities and another for their spatial attributes (so-called "what" and "where" pathways). We examined the spatio-temporal mechanisms along auditory "what" and "where" pathways and whether they are automatically engaged in differentially processing spatial and pitch information of identical stimuli. Electrical neuroimaging of auditory evoked potentials (i.e., statistical analyses of waveforms, field strength, topographies, and source estimations) was applied to a passive "oddball" paradigm comprising 2 varieties of blocks of trials. On "what" blocks, band-pass–filtered noises varied in pitch, independently of perceived location. On "where" blocks, the identical stimuli varied in perceived location independently of pitch. Beginning 100 ms poststimulus, the electric field topography significantly differed between conditions, indicative of the automatic recruitment of distinct intracranial generators. A distributed linear inverse solution and statistical analysis thereof revealed activations within superior temporal cortex and prefrontal cortex bilaterally that were common for both conditions, as well as regions within the right temporoparietal cortices that were selective for the "where" condition. These findings support models of automatic and intrinsic parallel processing of auditory information, such that segregated processing of spatial and pitch features may be an organizing principle of auditory function.

Keywords: auditory evoked potential, brain imaging, event-related potential, LAURA source estimation, "what" and "where" pathways

Introduction

Sounds convey information both about what they signify/identify as well as about where they are located in space. Anatomical, neuropsychological, psychophysical, hemodynamic neuroimaging, and electrophysiological evidence suggest that these functions are likely mediated by specialized brain networks.

The organization of auditory areas has been investigated both in humans (Rivier and Clarke 1997; Clarke and Rivier 1998; Morosan and others 2001; Tardif and Clarke 2001; Wallace and others 2002; Chiry and others 2003) and nonhuman primates (e.g., Kosaki and others 1997; Kaas and Hackett 2000) using anatomical, cytoarchitectonic, and immunohistochemical methods. The collective evidence supports a parallel and hierarchical organization wherein (at least) 2 interconnected pathways originate in the primary (also termed A1 or "core") auditory cortex (and perhaps also subcortically; Rauschecker and others 1997). One pathway projects from A1 caudally along the superior temporal cortex and into parietal cortices as well as dorsal subdivisions of frontal and prefrontal cortices, and a second pathway projects from A1 rostrally along the superior temporal cortex into ventral subdivisions of frontal and prefrontal cortices (e.g., Hackett and others 1999; Romanski and others 1999; Kaas and Hackett 2000, for review).

More recently, the particular functional attributes of these pathways have begun to be detailed. Sound recognition and localization functions appear to map onto the above-mentioned rostral–ventral and caudal–dorsal pathways, giving rise to the so-called "what" and "where" pathways, respectively. Electrophysiological recordings from lateral belt areas of rhesus monkeys indicate that neurons within anterior portions demonstrated preferential responses to specific vocalizations independent of their azimuthal position, whereas neurons within caudal portions demonstrated such preferentiality to position independent of the specific vocalization (Tian and others 2001; see also Rauschecker and others 1997; Recanzone and others 2000).

Three aspects of the seminal Tian and others (2001) study are worth noting, which highlight issues that remain unresolved in subsequent studies. First, a subgroup of neurons in both anterior and caudal portions demonstrated selectivity for both position and vocalization. Functional subdivisions may therefore be relative, rather than absolute. Second, because the time course of differential processing of location and vocalization information was not reported, the precise timing of differential processing along parallel streams as well as whether such functional pathways (if present) originate within temporal cortices or elsewhere remains unknown. Third, this study was performed on anesthetized animals under passive listening conditions, raising the questions of whether functional specialization within the auditory system proceeds automatically and whether the dynamics and networks contributing to such specialization are influenced by attention and task demands.

Data describing auditory "what" and "where" pathways in humans likewise remain largely controversial (e.g., Middlebrooks 2002; Hall 2003). Focal lesions can lead to behavioral deficits in either sound localization (following temporoparietal and dorsal frontal lesions) or recognition (following middle and anterior temporal and ventral frontal lesions), while leaving performance on the other task intact, suggestive of a strong degree of independence of these functions (Clarke and others 2000, 2002; see also Clarke and others 1998 for similar psychophysical evidence from healthy subjects on a short-term memory task). Similarly, hemodynamic imaging studies generally show that a sound recognition network includes activations within the superior and middle temporal gyri and inferior frontal gyri, whereas a sound localization network includes activations within the parietal lobule, parts of the premotor cortex, and the prefrontal cortex (Alain and others 2001; Maeder and others 2001; Arnott and others 2004; although see also Warren and Griffiths 2003, for evidence of differential processing within temporal cortex itself). Others,

however, have failed to observe differential activity when subjects selectively attended to the spectral or spatial features of pure tones (Zatorre and others 1994, 1999; Weeks and others 1999). Although some contend that spatial patterns of activations are truly selective (i.e., an area is involved in one function but not another; e.g., Maeder and others 2001), others interpret these signals as indicative of an alteration in the degree of response strength (e.g., Alain and others 2001). Regardless of the interpretation, however, the low temporal resolution of these techniques obfuscates the ability to differentiate "what" and "where" pathway activity that may manifest as truly selective at one point in time and as a change in relative strength at another point in time.

The spatiotemporal brain dynamics of auditory "what" and "where" functions have been addressed with electroencephalography (EEG) and magnetoencephalography (MEG). However, this is no consensus regarding the timing of the earliest differentiation of these functions. In one study, Alain and others (2001) used a delayed match-to-sample (DMS) task with stimulus pairs (noise bursts) and found the earliest task-related difference at 300 ms following onset of the first stimulus of the pair. Anourova and others (2001) also used a DMS task (with tones) but observed task-related effects on the latency and magnitude of the N1 component (80–110 ms) in response to presentation of the second stimulus of the pair. In contrast to Alain and others (2001), however, no effects of task were observed in the responses to the first stimulus of the pair. Most recently, Herrmann and others (2002) estimated equivalent current dipole (ECD) locations from MEG recordings 120–160 ms poststimulus onset during a target detection paradigm with meaningful sounds presented at any of 7 different simulated locations. They found that ECD coordinates within the right hemisphere, but not the left, were more lateral in response to blocks of trials requiring location discrimination than to those requiring semantic discrimination. By contrast, Anourova and others (2001) observed that ECD coordinates were more medial for location discrimination than for pitch discrimination. Still others have restricted their analyses to the mismatch negativity derivation without directly comparing responses with spatial and pitch information (e.g., Schröger and Wolff 1997; Ozaki and others 2004; Näätänen and others 2005 for review) or have focused instead on the conjunctive processing of pitch and location (e.g., Takegata and others 2001) or on differences between nonspatial auditory features such as pitch, intensity, and duration (e.g., Giard and others 1995; Levänen and others 1996).

Several major issues concerning auditory "what" and "where" pathways thus remain unresolved. The first concerns whether these pathways rely on distinct brain networks or whether functional specialization follows instead from the degree of activity within a common set of brain regions. Intertwined with this issue is the question of the dynamics of differential "what" and "where" activity. A second unresolved issue is whether differential brain activity along these pathways can be elicited independently of task demands—that is, automatically following passive listening. This is important for determining whether segregated processing is an organizing principle of the auditory system or rather emerges only as a consequence of attentional modulations that differentially affect recognition and spatial functions. This is likewise important for linking results across species where recordings have been made under passive listening conditions (and often under anesthesia).

The present study addressed these issues of the spatiotemporal brain dynamics of sound location and pitch processes and in particular whether and when these functions rely on distinct brain networks as well as whether differential processing occurs automatically. Evidence for such would support the view that "what" and "where" pathways constitute an intrinsic functional architecture within the auditory system of humans. We combined electrical neuroimaging techniques with a passive auditory "oddball" paradigm, varying across blocks of trials the probability of either the pitch or the perceived location of stimuli (see Table 1). Analyses were restricted to the direct comparison of frequently presented stimuli as these serve as the bases for mnemonic traces of both pitch and spatial information in this paradigm. These also avoids the confound—present in the analysis of rare stimulus presentations—of intermixing auditory afferent responses with those underlying mismatch responses (see Näätänen and others 2005 for review). We employed an electrical neuroimaging analysis approach capable of statistically differentiating changes in response strength from changes in the topography of the electric field at the scalp, the latter of which forcibly reflects changes in the configuration of brain generators.

Materials and Methods

Subjects

Twelve (7 men, 5 women) unpaid volunteers aged 20–34 years (mean age ± SD = 26 ± 4.5 years) provided written, informed consent to participate in the experiment. All procedures were approved by the Ethical Committee of the Faculty of Biology and Medicine of the University of Lausanne. Ten of the subjects were right handed, and the other 2 were left handed (Oldfield 1971). None of the subjects had current or prior neurological or psychiatric illnesses. All had normal or corrected-to-normal vision and reported normal hearing.

Stimuli and Procedure

Subjects watched a muted film during the experiment and received no instructions about the auditory stimuli until the psychophysical test immediately following the EEG portion (detailed below). Auditory stimuli were band-pass–filtered noise bursts (100-ms duration, 10-ms rise/fall, 44 100-Hz sampling). One stimulus had a 250-Hz center frequency ± 0.25 octave and the other a 500-Hz center frequency ± 0.25 octave. The perceived location within left or right hemispace was induced by an interaural time difference (ITD) of 800 μs, which led to a perceived lateralization approximately 90° from the central midline. Although the use of free-field stimuli or sounds lateralized according to the head-related transfer function has clear advantages, our choice of using ITD was motivated in large part by plans to apply this paradigm to clinical populations that demonstrate impaired processing of either ITD or interaural intensity difference cues (e.g., Yamada and others 1996).

Table 1

Experimental paradigm. Right- and left- sided stimuli were induced by an 800-μs interaural time difference. Only frequent stimuli were included in AEP analyses and were collapsed across blocks of the same type (see Materials and Methods for details)

Block type	Frequent stimuli (% occurrence)	Rare stimuli (% occurrence)
What	Left sided 250 Hz (40)	Left sided 500 Hz (10)
	Right sided 250 Hz (40)	Right sided 500 Hz (10)
What	Left sided 500 Hz (40)	Left sided 250 Hz (10)
	Right sided 500 Hz (40)	Right sided 250 Hz (10)
Where	Left sided 250 Hz (40)	Right sided 250 Hz (10)
	Left sided 500 Hz (40)	Right sided 500 Hz (10)
Where	Right sided 250 Hz (40)	Left sided 250 Hz (10)
	Right sided 500 Hz (40)	Left sided 500 Hz (10)

Stimulus intensity at the ear was approximately 76 dB sound pressure level (measured using a CESVA SC-160 sound pressure meter; www.cesva.com). Two spatial positions (one in the left hemispace and one in the right hemispace) and two pitch levels were used. In total, there were 4 stimuli whose relative frequency of presentation was used to generate 4 blocks of trials (see Table 1). Each block lasted approximately 15 min each and contained 800 trials. Stimuli were delivered via insert earphones (Etymotic model ER-4P; www.etymotic.com) with a pseudorandomized interstimulus interval of 700–1100 ms at steps of 100 ms, which was controlled using E-prime (www.pstnet.com/eprime). For blocks of trials designated "what," 80% of trials were of one pitch, irrespective of their perceived location in left or right hemispace, whereas the remaining 20% of trials were of the other pitch, again irrespective of their perceived location in the left or right hemispace. There were 2 "what" blocks to fully counterbalance which pitch was preponderant. For blocks of trials designated "where," 80% of the trials were at one perceived location, irrespective of their pitch, whereas the remaining 20% of trials were at the other perceived location, again irrespective of their pitch. As above, there were 2 "where" blocks to fully counterbalance which perceived location was preponderant. Only responses to the frequent trials (i.e., those presented 80% of the time within a block) were included in analyses. By collapsing across the 2 "what" blocks and 2 "where" blocks separately, we were able to compare responses with physically identical stimuli. That is, differences in brain responses could not be explained by acoustic differences in stimuli. Second, limiting our analyses to these frequent stimuli avoided any confounds due to novelty detection occurring for the remaining 20% of trials. The order of blocks was pseudorandomized across subjects. (All subjects also completed a separate psychophysical session with shortened blocks of trials, which confirmed that these stimuli could be easily and reliably differentiated in terms of pitch and location. Accuracy in deviance detection was always >95%.)

The rationale for this design is the following. To the extent that differential spatial and pitch processings are automatic and intrinsic to auditory processing in humans, the mnemonic traces established for the frequent stimuli should differ between blocks. That is, during the "what" blocks the majority of stimuli are of one pitch and a mnemonic trace is formed for it. Even though spatial position is also changing, the mnemonic trace for this feature is weaker (as would be supported by numerous investigations of auditory oddball paradigms). An equivalent, but converse situation occurs during the "where" blocks.

EEG Acquisition and Preprocessing

Continuous EEG was acquired at 512 Hz though a 128-channel Biosemi ActiveTwo AD-box (www.biosemi.com) referenced to the common mode sense (active electrode) and grounded to the driven right leg (passive electrode), which functions as a feedback loop driving the average potential across the electrode montage to the amplifier zero. Peristimulus epochs of EEG (–100-ms prestimulus to 500-ms post-stimulus onset) were averaged for each of the 2 stimulus conditions and from each subject to calculate auditory evoked potentials (AEPs). In addition to a ±100 μV artifact rejection criterion, EEG epochs containing eye blinks or other noise transients were removed. The average number (±SEM) of accepted EEG sweeps was 1037 ± 61 for the "what" condition and 987 ± 59 for the "where" condition. These values did not statistically differ (t_{11} = 1.15; P > 0.28). Prior to group averaging, data at artifact electrodes from each subject were interpolated (Perrin and others 1987). Likewise, data were baseline corrected using the 100-ms prestimulus period, band-pass filtered (0.68–40.0 Hz), and recalculated against the average reference.

General EEG Analysis Approach

Differences between auditory "what" and "where" processing were identified with a multistep analysis procedure, which we refer to as electrical neuroimaging, that uses local as well as global measures of the electric field at the scalp. This procedure and its benefits over standard waveform analyses have been described in detail elsewhere (e.g., Michel and others 2004; Murray and others 2004; Foxe and others 2005; Murray and others 2006; Murray and others 2005). Briefly, it entails analysis of response strength and response topography to differentiate effects due to modulation in the strength of responses of statistically indistinguishable brain generators from alterations in the configuration of these generators (vis-à-vis the topography of the electric field at the scalp) as well as latency shifts in brain processes across experimental conditions. In addition, we utilized a local autoregressive average (LAURA; Grave de Peralta and others 2001; Grave de Peralta Menendez and others 2004) distributed linear inverse solution to visualize the likely underlying sources of effects identified in the preceding analysis steps. Each analysis is briefly detailed here, below.

Waveform Modulations

A first level of analyses was conducted using area measures over the 100–200 ms from selected scalp locations (corresponding to F3, Fz, F4, C3, Cz, C4, P3, Pz, and P4 of the 10–20 system). This time range was selected based on the outcome of the pointwise paired *t*-tests described below and corresponds to the N1 component of the AEP, which has a characteristic frontocentral negative topography (e.g., Herrmann and others 2002). These area measures were submitted to a 2 × 3 × 3 repeated measures analysis of variance (ANOVA) using condition ("what," "where"), electrode position along the anterior–posterior direction (frontal, central, parietal), and electrode position in the left/right direction (left, midline, right) as within-subject factors.

To determine the timing of differences in AEP responses to "what" and "where" conditions, we calculated pointwise paired *t*-tests between AEP responses. By this method, we identified the timing of differential responses between conditions. For each electrode, the first time point where the *t*-test exceeded the 0.05 alpha criterion for at least 11 consecutive data points (>20 ms at a 512-Hz digitization rate; see, e.g., Guthrie and Buchwald 1991) was labeled as onset of an AEP modulation (see, e.g., Guthrie and Buchwald 1991; Murray and others 2002, 2004, for similar approaches). The results of the pointwise *t*-tests from the entire electrode montage are displayed as an intensity plot (Fig. 2*a*).

Field Strength Modulations

Changes in the strength of the electric field at the scalp were assessed using the global field power (GFP; Lehmann and Skrandies 1980) for each subject and stimulus condition. GFP is equivalent to the spatial standard deviation of the electric field at the scalp, yields larger values for stronger electric fields, and is calculated as the square root of the mean of the squared value recorded at each electrode (vs. average reference). A pointwise paired *t*-test using the variance across subjects statistically compared the "what" and "where" conditions (temporal criterion applied as above).

Topographic Modulations

To statistically identify periods of topographic modulation, we calculated the global dissimilarity (Lehmann and Skrandies 1980) between the "what" and "where" conditions for each time point of each subject's data. Global dissimilarity is an index of configuration differences between 2 electric fields that is independent of their strength (normalized data are compared). A Monte Carlo nonparametric bootstrapping procedure (Manly 1991) identified statistical differences in the global dissimilarity between the 2 conditions. Because electric field changes are indicative of changes in the underlying generator configuration (Lehmann 1987), this test provides a statistical means of determining if and when the brain network activated by "what" and "where" conditions differ.

Topographic Pattern Analysis

A pattern analysis of the event-related potential (ERP) scalp topography across time and experimental conditions was performed in order to determine whether topographic differences observed above using global dissimilarity were explainable by a single or multiple configuration changes, by a latency shift across conditions, or by some combination of these possibilities. First, a *k*-means cluster analysis (Pasqual-Marqui and others 1995) identified the most dominant scalp topographies appearing in the group-averaged ERPs from each condition over time. This approach is based on the observation that evoked potential topographies do not change randomly but rather remain for a period of time in a certain configuration and then switch to a new stable configuration (e.g., Lehmann 1987; Michel and others 2004). The optimal number of topographies or "template maps" that explains the

whole data set (i.e., both conditions collectively) was determined by a modified cross-validation criterion (Pasqual-Marqui and others 1995). Second, the pattern of the template maps identified in the group-averaged data was statistically tested in the data of individual subjects. To do this, template maps were compared with the moment-by-moment topography of the individual subject's data from each condition by means of strength-independent spatial correlation (see, e.g., Foxe and others 2005 for a recent detailed description, including formulae). For each time point, the AEP topography was compared with template maps and was labeled according to the one with which it best correlated. It is important to note that this labeling procedure is not exclusive, such that a given period of the data for a given subject and stimulus condition is often labeled with multiple template maps. This yields a measure of map presence that was in turn submitted to a repeated measure ANOVA with factors of condition and map (hereafter referred to as "fitting"). This fitting procedure revealed whether a given experimental condition was more often described by one map versus another, and therefore if different intracranial generator configurations better accounted for particular experimental conditions (i.e., if there is a significant interaction between factors of condition and map).

LAURA Source Estimation

We estimated the sources in the brain underlying the AEPs from each condition, using the LAURA distributed linear inverse solution (Grave de Peralta and others 2001; Grave de Peralta Menendez and others 2004; see Michel and others 2004, for a comparison of inverse solution methods). LAURA selects the source configuration that better mimics the biophysical behavior of electric vector fields (i.e., activity at one point depends on the activity at neighboring points according to electromagnetic laws). The solution space was calculated on a realistic head model that included 4024 nodes, selected from a 6 × 6 × 6–mm grid equally distributed within the gray matter of the Montreal Neurological Institute's average brain. The results of the above analyses defined time periods for which intracranial sources were estimated. Statistical analysis was conducted using a paired *t*-test at each node. Given that LAURA is a distributed source model, the issue arises of the possibility of obtaining spurious or "ghost" sources. A treatment of the validity of LAURA in terms of localization error is beyond the scope of the present study, though simulations and evaluations of empirical data exist (e.g., Michel and others 2004). We would instead note that determining the mean source estimation across subjects and furthermore statistically comparing these estimations provide one means of minimizing the likelihood of falsely accepting a ghost source as valid because the probability that a source is consistently observed across individuals and conditions is reasonably small.

Results

Electrophysiologic Results

AEP waveforms from a set of 9 frontal, central, and parietal scalp sites are displayed in Figure 1. Visual inspection of these waveforms shows that responses to physically identical stimuli differed between "what" and "where" conditions. Our first level of analysis compared area measures over the 100- to 200-ms poststimulus period from these electrodes (see Materials and Methods for details). This prototypical analysis of AEP waveforms is included here to assist the reader in relating results of the multistep electrical neuroimaging analyses to more historically traditional approaches. The ANOVA conducted on these area measures revealed a significant main effect of experimental condition ($F_{1,11} = 5.52$; $P < 0.04$). No other main effect met our 0.05 significance criterion (all P values >0.15). Of the interactions, those between condition and electrode position along the anterior–posterior axis and also between condition and electrode position along the left–right axis showed a trend toward significance ($F_{2,10} = 2.79$; $P = 0.10$, and $F_{2,10} = 3.42$; $P = 0.07$, respectively). All other interactions failed to meet our significance criterion ($P > 0.30$).

In order to more precisely characterize differential responses from the "what" and "where" conditions, AEP data from all channels were then submitted to the multistep analyses described in Materials and Methods, the results of which are displayed in Figure 2. The intensity plot of the pointwise *t*-tests

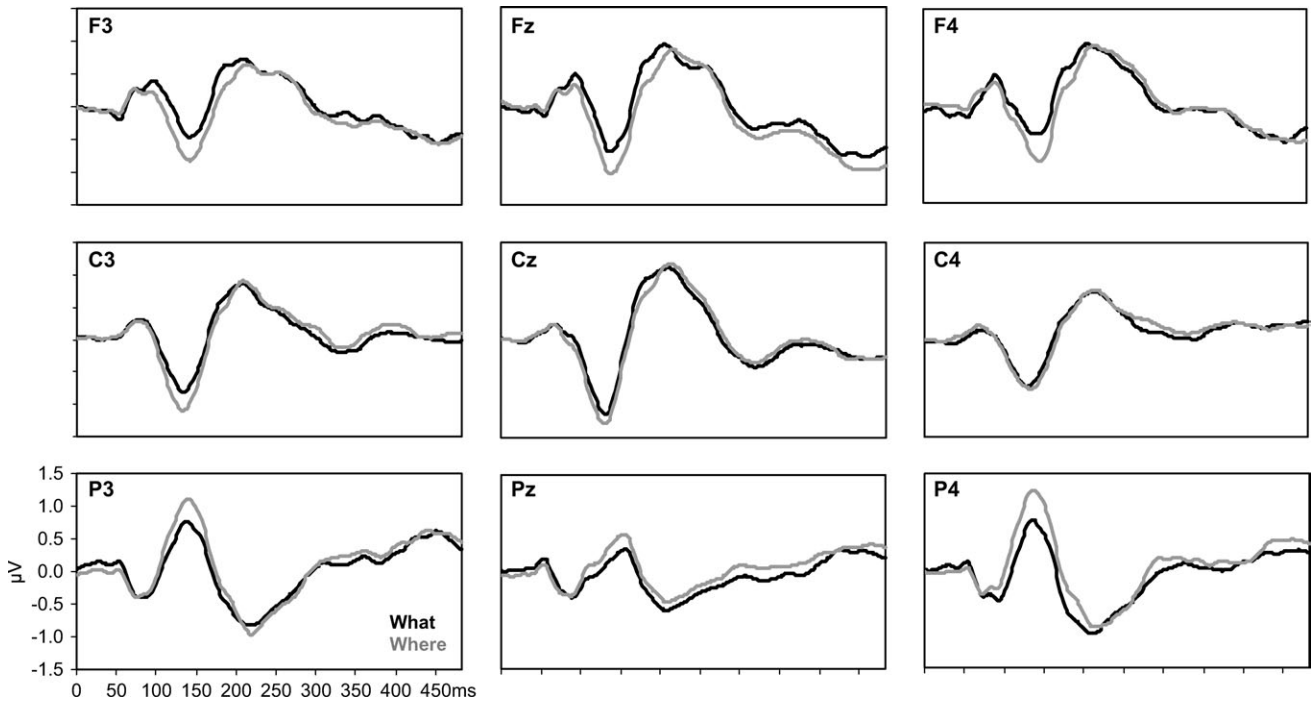

Figure 1. Group-averaged ($N = 12$) AEP waveforms from a subset of frontal, central, and parietal scalp locations. Black traces indicate responses to the "what" condition and gray traces the "where" condition. Scales are identical across all plots, and positive voltage is plotted upward.

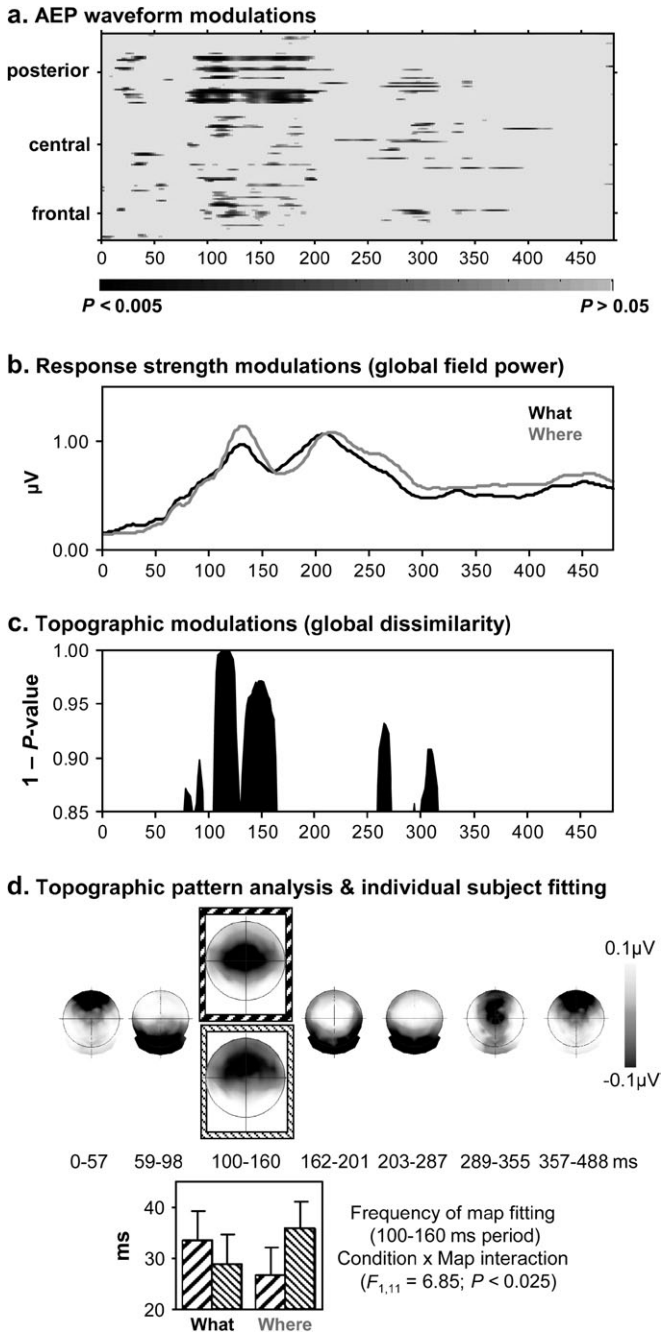

Figure 2. Electrical neuroimaging results (see Materials and Methods for details). (*a*) AEP waveform modulations were assessed with pointwise paired *t*-tests for each electrode and time point using the variance across subjects. Time is plotted along the *x*-axis, scalp electrode location along the *y*-axis, and the *P* value of these *t*-tests as a grayscale value. These tests revealed a temporally sustained response modulation over multiple scalp sites over the ~100- to 160-ms period. (*b*) Field strength modulations across time were assessed with GFP from each condition. No significant modulations in GFP were observed. (*c*) Differences in the electric field topography at the scalp between experimental conditions were statistically tested using global dissimilarity, and the results are displayed here as 1 minus the *P* value as a function of time poststimulus onset. Significant differences between experimental conditions were observed over the ~100- to 160-ms period. (*d*) A topographic pattern analysis revealed that 8 different maps accounted for the cumulative group-averaged data set from both conditions, which are shown here as a function time (left hemiscalp leftward and nasion upward). Except for the 100- to 160-ms period, the same sequence of maps was observed in the group-averaged AEPs from both conditions. Over this time period, however, different maps were ascribed to different experimental conditions. This was statistically tested through the individual subject-fitting procedure, the results of which are shown in the bar graph depicting the frequency with which each of these 2 template maps was observed over the 100- to 160-ms period. Patterns used in the bar graph correspond to the frames surrounding different topographic maps. There was a significant interaction between map and condition, indicating that different maps better accounted for the responses from each condition.

across the electrode montage revealed robust and widespread differences between experimental conditions over the ~100- to 200-ms period (Fig. 2*a*). Effects prior to this latency failed to meet our temporal criterion (i.e., <20-ms duration) and occurred at a limited number of scalp sites. In contrast to analyses of individual electrodes, analysis of the GFP provided no indication of significant modulations in response strength between "what" and "where" conditions during the poststimulus period (Fig. 2*b*). However, analysis of the global dissimilarity between these conditions revealed significant topographic differences over the ~109- to 160-ms period, indicative of the activation of distinct configurations of intracranial brain generators for each experimental condition (Fig. 2*c*). We would emphasize that topographic modulation need not also manifest as a change in the GFP. Rather, these are 2 complimentary measures of the electric field at the scalp.

A topographic pattern analysis (see Materials and Methods) was then conducted to determine whether response differences between conditions followed from single or multiple electric field configuration changes over this time period or alternatively whether such followed from a latency shift between conditions. Eight different template maps accounted for the collective group-averaged data set (the global explained variance was 95.45), which are shown in Figure 2*d*. Moreover, this analysis further suggested that single, distinct template maps better accounted for the ~100- to 160-ms period of the responses to "what" and "where" conditions. This pattern observed in the group-averaged data was tested in the data of individual subjects, using the above-mentioned fitting procedure (see Materials and Methods). The values of the fitting procedure were then submitted to a repeated measure ANOVA using stimulus conditions and template maps as within-subject factors (see bar graphs in Fig. 2*d*). There was a significant interaction between factors of condition and map over the 100- to 160-ms period ($F_{1,11}$ = 6.85, P < 0.025), indicating that each condition was better fit by different template maps. Neither main effect of condition nor that of map reached our significance criterion. As will be followed in the Discussion in detail, this series of analyses indicate that responses to "what" and "where" conditions differ at ~100 ms due to the stable engagement of distinct intracranial generator configurations (i.e., one template better described responses to pitch cues and another map better described those to location cues).

To this point, analyses at global and local levels revealed differential activity for "what" and "where" processing over the 100- to 160-ms period that was explained by a change in the topography of the electric field at the scalp (and by extension, the configuration of intracranial generators). Single, stable template maps accounted for this topographic modulation, rather than several different alterations in the electric field at the scalp. This pattern of results is most parsimoniously interpreted as the activity of one configuration of active brain regions for the "what" condition and a different configuration for the "where" condition. LAURA distributed source estimations were therefore calculated over the 100- to 160-ms period. To do this, AEPs for each subject and each experimental

condition were separately averaged across time (i.e., when stable topographies were identified). Source estimations were then calculated and subsequently averaged across subjects. Figure 3 shows the mean LAURA estimations over the 100- to 160-ms period. Both conditions exhibited prominent sources within the posterior superior temporal cortex and prefrontal cortex, bilaterally. The "where" condition also included prominent sources within the right inferior parietal and temporoparietal cortices. Statistical comparison of these LAURA source estimations revealed that 3 foci within the right hemisphere were significantly ($t_{11} \geq 2.9$; $P \leq 0.015$) more active in the "where" than in the "what" condition. These included the superior parietal lobule (maximum at 30, –55, 60 mm using the coordinate system of Talairach and Tournoux 1988; corresponding to Brodmann area 7), the inferior parietal lobule (maximum at 53, –42, 26 mm; Brodmann area 40), and the temporoparietal junction (maximum at 44, –70, 26 mm; Brodmann area 39). No regions were significantly more active for the "what" than for the "where" condition.

Discussion

Differential processing of physically identical spatial and pitch information occurs preattentively via a single, stable topographic modulation in the electric field at the scalp, beginning at ~100 ms poststimulus onset. This is indicative of the automatic engagement of distinct cortical auditory "what" and "where" functional networks. Distributed linear source estimations (LAURA) during this time period revealed activations within the superior temporal cortex and prefrontal cortex bilaterally that were common for both "what" and "where"

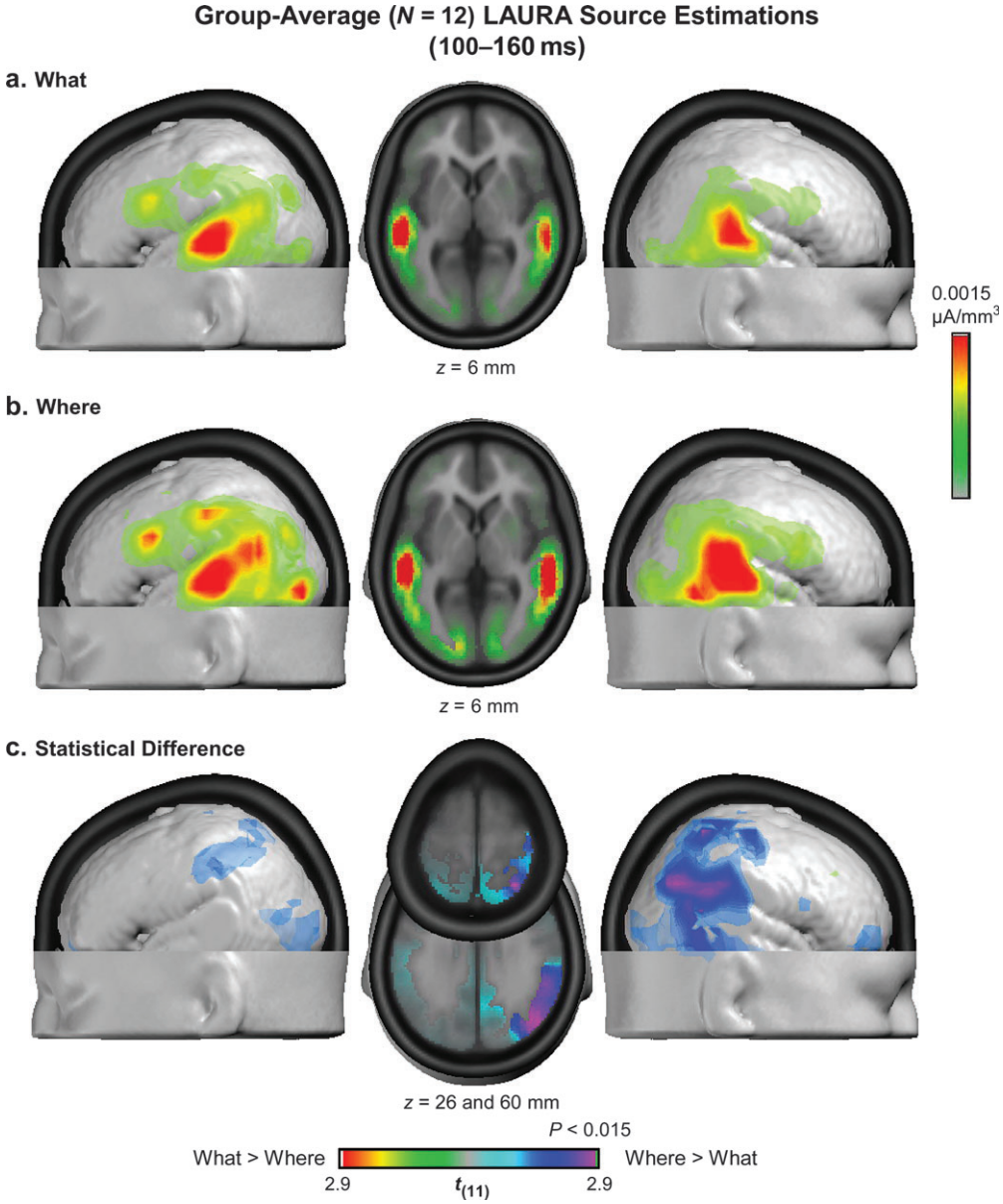

Figure 3. LAURA source estimations over the 100- to 160-ms period. (*a*, *b*) Group-averaged ($N = 12$) source estimations for each stimulus condition are shown on a 3-dimensional rendering of the MNI template brain as well as on axial slices (Talairach and Tournaux *z*-coordinate indicated; left hemisphere on left side) where source estimation maxima were obtained. (*c*) Statistical comparison of the source estimations shown in (*a*) and (*b*). Color indicates the t_{11} values and corresponding *P* values.

conditions. In addition, statistical analysis of these source estimations identified regions within the right temporoparietal cortices that were selectively active for the "where" condition. These latter results are in agreement with prior evidence of right-hemisphere lateralized auditory spatial processing. The collective data support the hypothesis that (partially) segregated processing is an underlying principle of functional organization in auditory cortices.

This study constitutes the first electrical neuroimaging demonstration in humans detailing the differences in the spatiotemporal mechanisms of preattentive auditory pitch and spatial processing. A major advance of the present study was to apply a multistep analysis procedure that permits statistically based neurophysiological interpretations of differences between auditory "what" and "where" processing observed in the scalp-recorded data. Based solely on these analyses of the surface-recorded data, our results provide a statistical basis for asserting that auditory "what" and "where" processing engage (partially) distinct and stable configurations of intracranial generators preattentively and beginning ~100 ms poststimulus onset. This conclusion is in solid agreement with previous hemodynamic imaging (e.g., Maeder and others 2001) and neuropsychological studies (e.g., Clarke and others 2000, 2002) that support (at least partially) segregated networks for these functions and contrasts with the conclusion that differences in these functions derive from modulations in the degree of activity within a common network (Alain and others 2001). In addition to this conclusion based on analyses of the surface-recorded data, statistical analysis of the source estimations using the LAURA distributed linear inverse solution indicates that regions within the right parietal and temporoparietal cortices are selectively involved in auditory spatial processing over the 100- to 160-ms period. This finding is not altogether novel. Numerous groups have now observed responses in these regions of humans and nonhuman primates in response to spatial features of sounds or spatial discrimination of sounds (e.g., Stricanne and others 1996; Griffiths and others 1997, 1998; Bushara and others 1999; Weeks and others 1999; Kaiser and others 2000; Alain and others 2001; Maeder and others 2001; Zatorre and Penhune 2001; Lewald and others 2002; Ducommun and others 2002, 2004; Arnott and others 2004; Palomäki and others 2005; see also Tervaniemi and Hugdahl 2003 for review), which in many cases have been lateralized to the right hemisphere. Lesions to these regions likewise result in selective deficits in spatial functions, while leaving recognition functions intact (e.g., Griffiths and others 1997; Clarke and others 2000, 2002). The right-lateralized differential effects between "what" and "where" conditions observed in the present study are highly consistent with the results of Herrmann and others (2002) and Anourova and others (2001), despite differences in the precise localization. By analyzing the coordinates of ECD models, these earlier studies claimed that functional segregation arises within the superior temporal plane itself. However, as in the case of AEP waveform analyses, some commentary on ECD source estimations is worthwhile. Although statistical analysis of the location and strength of ECDs is sophisticated and can provide some information regarding differences in the configuration of intracranial generators between conditions, this particular source model represents a center of mass of the implicated brain network rather than information on the (differential) distributed network, particularly because the number (and often the location) of ECDs is predefined by the experimenter. Thus, a difference in ECD coordinates need not forcibly reflect a generator difference at the location of the ECD itself. It is also important to note that ECD parameters are several degrees removed from the actual surface-recorded data (i.e., a source model and its assumptions are used to generate the analyzed data). Consequently, prior EEG/MEG studies could not resolve the precise timing and mechanism of differential "what" and "where" processing. Rather, a likely explanation for the difference in ECD coordinates between "what" and "where" conditions in these prior studies is that the "where" condition selectively activates parietal and temporoparietal cortices and therefore shifts the center of mass of the ECD model.

It is also worth noting that the timing of these effects is highly similar to those obtained by Herrmann and others (2002) using an active discrimination task with environmental sounds. One implication is that differential "what" and "where" processing is likely not influenced (at least at its initial stages) by task demands or by the use of band-pass–filtered noises (present study) versus environmental sounds (Herrmann and others 2002). By contrast, we are reluctant to assert that the present effects represent the earliest possible functional differentiation. That is, the present effects occur some 80 ms later than the ~15–20 ms reported for response onset within primary auditory cortex (e.g., Liegeois-Chauvel and others 1994; Howard and others 2000; Godey and others 2001; Brugge and others 2003). In addition, recent evoked magnetic field recordings from humans listening to monaural clicks further indicate that response propagation within the initial ~50-ms poststimulus includes regions of the anterolateral part of Heschl's gyrus, the posterior parietal cortex, posterior and anterior portions of the superior temporal gyrus, as well as the planum temporale (Inui and others 2005). In light of such information, the widespread network observed in the present study ~100 ms poststimulus onset is well within physiological plausibility. Nonetheless, future experimentation, involving intracranial microelectrode recordings from humans, would be necessary to affirm whether differential "what" and "where" processing is also apparent at earlier latencies and/or within subdivisions of the superior temporal plane.

Such notwithstanding, the present demonstration of preattentive differential processing of auditory spatial and pitch features does facilitate translational links between results obtained in humans and nonhuman primates because active discrimination tasks have thus far been used in studies of "what" and "where" processing in humans (with the exception of a passive follow-up experiment in Maeder and others 2001) and only passive tasks have been utilized in nonhuman primates. Still, analyses of the timing of differential processing will also be critical for interpreting effects observed in nonhuman primates. That is, although evidence of functional specialization within anterior and caudal lateral belt regions has been reported (Tian and others 2001), it is not clear whether effects within these subdivisions of the superior temporal plane constitute the earliest functional segregation along "what" and "where" pathways or potentially the consequence of feedback modulations. Resolving such issues will be important for future research aimed at the fuller integration of results across species and the determination of whether "what" and "where" pathways represent an automated and intrinsic functional infrastructure within the auditory system. The present study, however, does provide evidence that the cortical auditory system of humans is capable of segregated and parallel processing of spatial and pitch

information within the initial ~100-ms poststimulus onset within regions of the right temporoparietal cortices.

Notes

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