Task-modulated "what" and "where" pathways in human auditory cortex

Jyrki Ahveninen*†‡§, Iiro P. Jääskeläinen*‡, Tommi Raij*, Giorgio Bonmassar*, Sasha Devore¶, Matti Hämäläinen*, Sari Levänen*, Fa-Hsuan Lin*, Mikko Sams‡, Barbara G. Shinn-Cunningham¶, Thomas Witzel*, and John W. Belliveau*

*Harvard Medical School–Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Charlestown, MA 02129; †BioMag Laboratory, Helsinki University Central Hospital, FIN-00029, Helsinki, Finland; ‡Laboratory of Computational Engineering, Helsinki University of Technology, 02150, Espoo, Finland; and ¶Hearing Research Center, Boston University, Boston, MA 02215

Edited by Leslie G. Ungerleider, National Institutes of Health, Bethesda, MD, and approved August 1, 2006 (received for review December 5, 2005)

Human neuroimaging studies suggest that localization and identification of relevant auditory objects are accomplished via parallel parietal-to-lateral-prefrontal "where" and anterior-temporal-to-inferior-frontal "what" pathways, respectively. Using combined hemodynamic (functional MRI) and electromagnetic (magnetoencephalography) measurements, we investigated whether such dual pathways exist already in the human nonprimary auditory cortex, as suggested by animal models, and whether selective attention facilitates sound localization and identification by modulating these pathways in a feature-specific fashion. We found a double dissociation in response adaptation to sound pairs with phonetic vs. spatial sound changes, demonstrating that the human nonprimary auditory cortex indeed processes speech-sound identity and location in parallel anterior "what" (in anterolateral Heschl's gyrus, anterior superior temporal gyrus, and posterior planum polare) and posterior "where" (in planum temporale and posterior superior temporal gyrus) pathways as early as ≈70–150 ms from stimulus onset. Our data further show that the "where" pathway is activated ≈30 ms earlier than the "what" pathway, possibly enabling the brain to use top-down spatial information in auditory object perception. Notably, selectively attending to phonetic content modulated response adaptation in the "what" pathway, whereas attending to sound location produced analogous effects in the "where" pathway. This finding suggests that selective-attention effects are feature-specific in the human nonprimary auditory cortex and that they arise from enhanced tuning of receptive fields of task-relevant neuronal populations.

functional MRI | magnetoencephalography | selective attention | spatiotemporal brain imaging

One's ability to perceive auditory objects in everyday acoustic environments depends on localization and identification of relevant sounds. Primate models (1, 2) suggest that this task is accomplished via parallel anterolateral "what" and caudolateral "where" nonprimary auditory cortex streams, resembling the functional subdivisions of the visual system (3, 4). Human neuropsychological (5–8) and neuroimaging (9–20) studies have consistently shown anterior-temporal-to-inferior frontal "what" and parietal-to-lateral-prefrontal "where" auditory pathways, but whether such dual pathways exist also in the human nonprimary auditory cortex has remained a more controversial issue. Although there is accumulating evidence that nonprimary auditory cortex regions posterior to the Heschl's gyrus (HG) are involved in spatial processing (21–26) and that areas anterior to HG process sound-identity cues such as speech (27, 28) and pitch (29), the posterior nonprimary auditory cortex areas have been reported to respond strongly to phonetic stimuli as well (30, 31). This observation has raised hypotheses alternative to the dual pathway model, suggesting that the posterior nonprimary auditory cortex processes rapid spectrotemporal changes (30, 32), common to both speech sounds and sound motion/location cues (32), and that the anterior pathway concentrates on invariant sound features (32). Evidence of a double dissociation between processing of phonetic vs. spatial features is thus needed to determine whether the dual pathway model is valid for anterior vs. posterior human nonprimary auditory cortex areas.

Selective attention is known to support both sound localization and recognition, but it is unclear how representations of auditory space and identity are top-down modulated in the human auditory cortex. Overall enhancement of human auditory cortex activity by selective attention has been verified by functional MRI (fMRI) (14, 33–37), positron emission tomography (38–40), electroencephalography (41), and magnetoencephalography (MEG) (42) studies, and recent fMRI results further implied that these effects mainly occur in the nonprimary auditory areas (37). Dichotic listening studies of spatial attention suggest signal enhancements in auditory areas contralateral to the attended ear (38, 42, 43). However, although distinct prefrontal and parietal activations to attentional processing of "what" vs. "where" auditory information have been consistently reported (9, 13–16), previous positron emission tomography and fMRI studies have failed to find evidence for feature-specific attentional effects for sound identity and location in the auditory cortex (37, 39). Whereas detailed neuronal mechanisms, including amplification of relevant object representations (44) and enhanced selectiveness for attended stimuli (45), have been characterized in the human visual cortices (see also refs. 4 and 46), it remains unclear how selective attention affects neuronal representations of sounds to facilitate auditory perception. Recent animal models suggested task-dependent modulation of spectrotemporal receptive fields in the auditory cortex (47), but such effects have so far not been shown in humans.

Functional neuroimaging of human auditory cortex is challenging because of its relatively small size. However, recent studies suggest that rapid attenuation of neuronal activity after two or more successive auditory stimuli, termed "neuronal adaptation" (48, 49), can be used to probe the selectivity of auditory cortex neurons for a particular type of information (50, 51), helping circumvent limited resolution of noninvasive neuroimaging methods. To measure stimulus-feature tuning properties of the human auditory cortex, one can vary the physical similarity between a pair of sounds (Adaptor and Probe) and measure the adaptation of a response as a function of the difference between the sounds (51). Specifically, a Probe sound

Author contributions: J.A., I.P.J., G.B., M.S., B.G.S.-C., and J.W.B. designed research; J.A., I.P.J., T.R., S.D., S.L., and F.-H.L. performed research; M.H., T.W., and J.W.B. contributed new reagents/analytic tools; J.A., I.P.J., T.R., M.H., and S.L. analyzed data; and J.A., I.P.J., and J.W.B. wrote the paper.

The authors declare no conflict of interest.

This paper was submitted directly (Track II) to the PNAS office.

Abbreviations: ECD, equivalent-current dipole; fMRI, functional MRI; HG, Heschl's gyrus; MEG, magnetoencephalography; ROI, region of interest; STG, superior temporal gyrus; PT, planum temporale; PP, planum polare.

§To whom correspondence should be addressed at: Martinos Center, Massachusetts General Hospital/Harvard Medical School/Massachusetts Institute of Technology, CNY 149 13th Street, Charlestown, MA 02129. E-mail: jyrki@nmr.mgh.harvard.edu.

www.pnas.org/cgi/doi/10.1073/pnas.0510480103

produces a strongly attenuated, i.e., adapted response after a physically identical Adaptor. Furthermore, if Adaptor and Probe differ in one sound attribute, adaptation is more prominent in a neuronal population broadly tuned (i.e., nonselective) than in a population sharply tuned (i.e., selective) to that attribute (50). Interestingly, visual selective attention appears to modulate adaptation of fMRI signals (45), suggesting that the phenomenon of adaptation can also be used to probe the neural basis of selective attention.

Neuronal adaptation in the human auditory cortex can be measured with the N1 response, peaking at ≈100 ms after stimulus onset in trial-averaged MEG. The N1 "adaptation cycle" is closely coupled with the cellular-level "very long" adaptation time constant of 1–10 s, purportedly necessary for representing temporally distributed auditory objects (49). Importantly, the N1 response has separate anterior and posterior auditory cortex sources (50, 52, 53). These sources adapt differently to sound-feature changes, the anterior source showing sharp and the posterior source showing broad frequency tuning (50). Given the necessity of fine frequency analysis for sound-object processing and our dependency on broadband spectral cues in auditory localization (54), these two N1 sources could reflect the "what" and "where" pathways of the human nonprimary auditory cortex.

We hypothesized that the human nonprimary auditory cortex includes parallel anterior "what" and posterior "where" pathways (1, 2), and that selective attention to sound identity vs. location modulates these pathways in a task-dependent fashion. We further hypothesized that these effects would be revealed by differential adaptation in the putative "what" and "where" auditory streams ≈100 ms after stimulus (50), as measured by a spatiotemporal brain imaging approach that combines the temporal resolution (milliseconds) of MEG with the spatial resolution (millimeters) of fMRI.

Results

Fig. 1 shows the stimulus/task paradigm used in the fMRI and MEG measurements. The reaction times (mean ± SEM) were not significantly different between the Attend Location (740 ± 75 ms) and Attend Phoneme (706 ± 70 ms) conditions, but the hit rate was higher [$F(1,8) = 28.8$, $P < 0.01$] in the Attend Phoneme (92 ± 3%) than Attend Location (83 ± 3%) condition. The false alarm rate to "sham targets" (i.e., a phonetic target during Attend Location condition and vice versa; $P = 0.12$) was slightly higher [$F(1,8) = 9.7$, $P < 0.05$] in Attend Location (5 ± 1%) than Attend Phoneme (1 ± 1%) condition. During the Ignore condition, the rate of false responses (0.6 ± 0.3%) was not significantly different from 0%.

Differential Adaptation to Phonetic vs. Spatial Information in Auditory Cortex. To test our first hypothesis of differential adaptation to "what" and "where" information in the anterior vs. posterior auditory cortex, we compared brain responses to Probes preceded by identical, phonetically different, or spatially different Adaptors (see Fig. 1*c* for a schematic illustration of response adaptation). In support of our hypothesis, the fMRI-weighted MEG source estimates (Figs. 2 and 3) showed that, although the auditory cortex activity to Adaptors was similar in all conditions, for Probe responses the main effect of stimulus change [$F(2,16) = 11.5$, $P < 0.01$] and the interaction of stimulus change and source location [$F(2,16) = 15.9$, $P < 0.001$] were significant. (The ANOVA effects of hemisphere laterality were nonsignificant.) Specifically, regions posterior to HG, including the planum temporale (PT) and posterior aspects of the superior temporal gyrus (STG), responded more strongly to Probes preceded by spatially different (but phonetically similar) Adaptors, in comparison to those preceded by phonetically different or identical Adaptors [right hemisphere: $F(1,8) = 16.3$, $P < 0.01$; left hemisphere: $F(1,8) = 20.2$, $P < 0.01$]. That is, activity in the posterior nonprimary auditory cortex was adapted less after location than phoneme changes (Figs. 2 and 3), suggesting that this region is more sharply tuned to spatial than phonetic information. In contrast, the anterior nonprimary auditory cortex regions, encompassing the anterolateral HG and parts of the anterior STG and the planum polare (PP), exhibited stronger activity when Adaptor and Probe differed phonetically than spatially, suggesting sharper phoneme tuning within these areas [right hemisphere: $F(1,8) = 11.2$, $P < 0.05$; left hemisphere: $F(1,8) = 20.4$, $P < 0.01$] (Figs. 2 and 3).

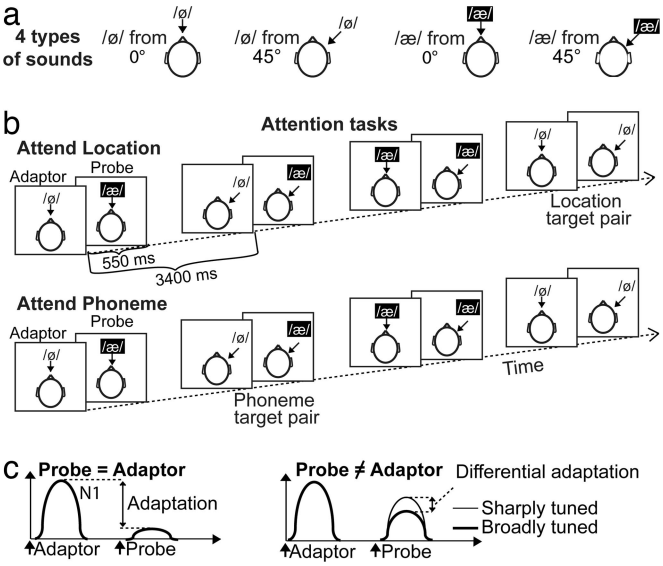

Fig. 1. Schematic illustration of the experimental paradigm and phenomenon of neuronal adaptation. (*a*) Sound stimuli. Pairs of Finnish vowels/æ/ and/ø/were presented from straight ahead or 45° to the right. (*b*) Sound sequence and tasks. Vowel pairs (i.e., Adaptor followed by Probe) were spatially discordant, phonetically discordant, or identical. During consecutive blocks, subjects were instructed to attend to either spatial (Attend Location) or phonetic (Attend Phoneme) similarities between successive sound pairs or to ignore the presented stimuli (Ignore condition not shown here). In the Attend Location condition, the subject responded to sound pairs that matched the spatial pattern of the preceding sound pair (same directions in same order), irrespective of the phonetic content. In the Attend Phoneme condition, the targets were, in turn, sound pairs being phonetically similar to the preceding sound pair (same phonemes in same order), irrespective of the spatial content. (*c*) Schematic illustration of response adaptation. A Probe sound preceded by an identical Adaptor produces a strongly adapted response. Adaptation is weakest when Probe differs from Adaptor in a feature to which the neuronal population is sharply tuned.

Selective Attention and Phoneme vs. Location Processing in Auditory Cortex. Our second hypothesis was that selective attention to phonetic vs. spatial features differentially modulates adaptation in the anterior "what" vs. posterior "where" auditory pathways, respectively. To quantify this, we modeled the anterior and posterior N1 sources (50, 53) as equivalent-current dipoles (ECD), which are less sensitive to crosstalk across different sources (e.g., anterior and posterior N1) than distributed estimates (55). Consistent with previous observations (50, 52, 53), the Adaptor N1 responses were explained by an earlier (left hemisphere, 92 ± 4 ms; right hemisphere, 89 ± 3 ms) posterior and a later (left hemisphere, 118 ± 4 ms; right hemisphere, 120 ± 5 ms) anterior ECD (see *Supporting Results* in *Supporting Text*, which is published as supporting information on the PNAS web site). Fig. 4 shows that these ECD loci, with significantly different origins along the anterior–posterior *y* axis in both hemispheres [$F(1,8) = 164.3$, $P < 0.001$], were in agreement with

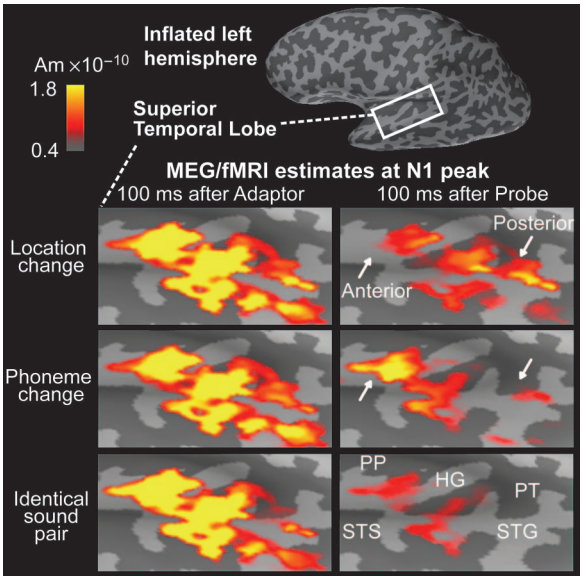

Fig. 2. Differential adaptation to phonemes vs. sound locations in nonprimary auditory cortex. Cortical fMRI-weighted MEG source estimates are shown in a representative subject at the N1 peak latency. The auditory cortex areas activated by the Adaptor (the first stimulus of the pair) are identical across the conditions, but specific adaptation-induced differences in activity patterns elicited by Probes (the second stimulus of the pair) are observed: The posterior activity is strongest (i.e., least adapted) when Adaptor and Probe differ spatially, and the anterior activity is strongest when Adaptor and Probe differ phonetically. The results were similar in the right hemisphere of this subject (not shown here). STS, superior temporal sulcus.

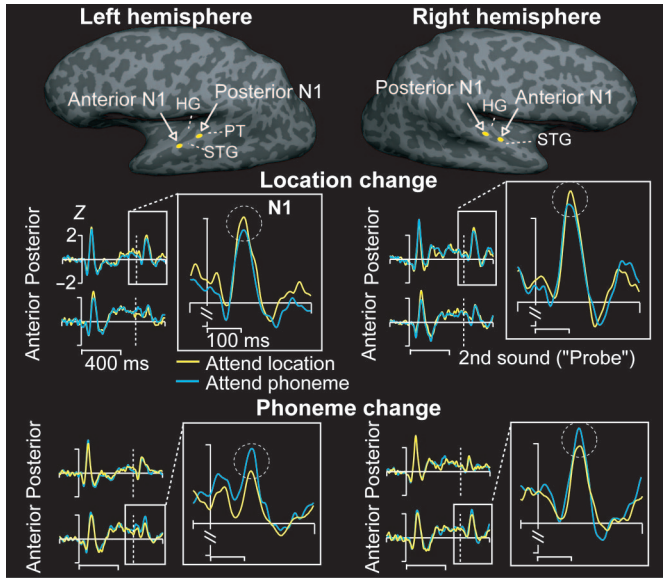

Fig. 4. Group-average ECD results of the two N1 subcomponents (50, 52, 53) showing the attentional modulation of the anterior and posterior auditory cortex activity to Probes following spatially or phonetically different Adaptors. The ECD locations (*Top*), group-averaged in a spherical standard space (60), are displayed on the inflated brain hemispheres of one subject. (*Middle* and *Bottom*) The source waveforms were amplitude-normalized within each subject before calculating the group averages (shown as *Z*-score values). This procedure retains the within-subject amplitude proportions, and each subject contributes equally to the group mean. *Insets* demonstrate the responses at −50–400 ms around Probes from sources showing peak attention effects. The N1 response amplitudes to Probes (encircled) are modulated task-dependently. The posterior N1 activity to Probes following spatially different Adaptors is enhanced by spatial attention. The anterior N1 activity to Probes following phonetically different Adaptors is enhanced by phonetic attention.

the fMRI-weighted MEG source estimates of N1 activity (Figs. 2 and 3). These ECD sources were used to model attentional modulation of feature-specific adaptation in the anterior and posterior nonprimary auditory cortex.

The ECD analysis corroborated the fMRI-weighted MEG results, suggesting differential adaptation to "what" vs. "where" information in the anterior and posterior regions of nonprimary auditory cortex (see *Supporting Results*). Furthermore, supporting our attentional hypothesis, there was a significant interaction [$F(2,16) = 4.4$, $P < 0.05$] among the type of attention (Attend Location vs. Attend Phoneme vs. Ignore), source location (anterior vs. posterior nonprimary auditory cortex), and stimulus order (Adaptor vs. Probe) (Figs. 4 and 5). Thus, selective attention modulated feature adaptation of anterior and posterior N1 responses to Probes in a task-specific fashion, without affecting the responses to Adaptors themselves. Based on *a priori* comparisons of means, the right-hemispheric posterior N1 response to Probes, when preceded by spatially different Adaptors, was significantly stronger in Attend Location vs. other conditions [$F(1,8) = 30.7$, $P < 0.01$]. That is, spatial attention reduced response adaptation to sound pairs with location changes in the putative "where" pathway in the right hemisphere. When phonetic attributes were attended, the anterior N1 activation to

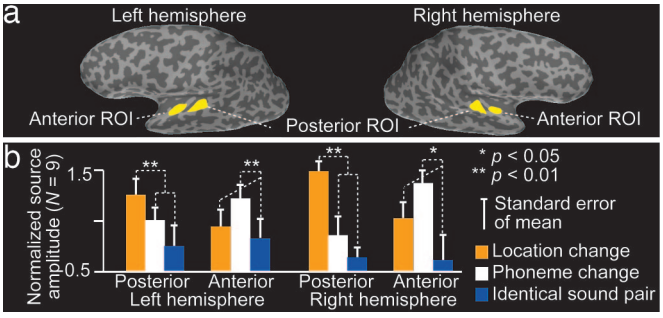

Fig. 3. ROI analysis of fMRI-weighted MEG source estimates to Probe sounds, showing differential adaptation after location vs. phoneme changes in the posterior and anterior auditory cortex, respectively. (*a*) The ROI locations in a representative subject are represented on the inflated cortex. (*b*) The ROI group average results suggest sharper spatial tuning in the posterior and sharper phoneme tuning in the anterior auditory cortex regions. The statistical significances refer to *a priori* Helmert contrast between the condition of interest (Location Change in the posterior and Phoneme Change in the anterior ROI) vs. other conditions.

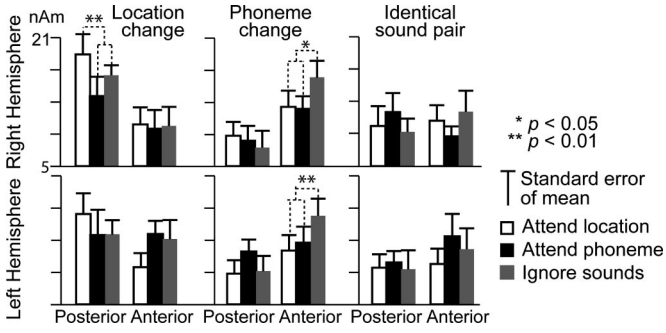

Fig. 5. Group-average selective attention effects in the right (*Upper*) and left (*Lower*) auditory cortices in ECD estimates. The response amplitudes to Probes are modulated task-dependently: The posterior N1 activity is enhanced by spatial attention, and the anterior N1 activity is enhanced by phonetic attention. The figure also shows the differential adaptation in the anterior and posterior N1 sources for phonetic vs. spatial information, respectively.

Probes preceded by phonetically different Adaptors was significantly enhanced in comparison to the other attentional conditions [left hemisphere: $F(1,8) = 13.3, P < 0.01$; right hemisphere: $F(1,8) = 8.2, P < 0.05$]. Hence, phonetic attention selectively reduced response adaptation to sound pairs with phonetic changes in the putative "what" pathway.

The hemisphere effects remained nonsignificant, yet a slight tendency of more prominent phonetic attention effects in the left vs. right anterior sources was observed, and the *a priori* comparisons of means showed significant spatial attention effects specifically in the right posterior N1 source (Figs. 4 and 5).

Relative Timing of Posterior and Anterior Auditory Pathways. There was a highly significant [$F(1,8) = 70.7, P < 0.001$] latency difference between the posterior (95 ± 2 ms; pooled across the hemispheres) and anterior (127 ± 3 ms) ECD-modeled N1 responses to Probe stimuli. This effect was also significant [$F(1,7) = 6.3, P < 0.05$] in fMRI-weighted MEG estimates of N1 activity, which peaked earlier in the posterior (106 ± 3.4 ms) than anterior (112 ± 2.7 ms) auditory cortex sources.

fMRI Results. Significant activations were found in and around the auditory cortices (extending from HG to STG, PT, PP, and the superior temporal sulcus) and in the frontal and parietal lobes (*Supporting Results*). According to the region of interest (ROI) analysis, selective attention significantly increased percent-signal changes in the auditory cortices and in the parietal and frontal lobe regions. The right parietal and prefrontal regions showed stronger activation during the Attend Location than Attend Phoneme condition, and there was a trend toward similar effects in the posterior nonprimary auditory cortex ROIs (see *Supporting Results*, Fig. 6, and Table 1, which are published as supporting information on the PNAS web site).

Discussion

Our results describe task-modulated anterior "what" and posterior "where" pathways in the human nonprimary auditory cortex. Consistent with previous findings of anterolateral "what" and caudolateral "where" nonprimary auditory cortex streams in the macaque (1, 2), our fMRI-weighted MEG source estimates suggest that the anterolateral HG, parts of the anterior STG, and PP process auditory object identity and that regions posterior to HG, including parts of PT and posterior STG, process sound location features (see Fig. 2). Manipulation of phonetic vs. spatial differences within sound pairs reveals a double dissociation of feature-specific adaptation between these anterior "what" vs. posterior "where" areas ≈70–150 ms from sound onset, and this effect is enhanced by selective attention (see Fig. 4). This attentionally modulated double dissociation extends previous evidence of parallel auditory "what" and "where" pathways, which has been more harmonious regarding areas beyond (5–20) than within (refs. 21–29; see also refs. 30 and 32) the human nonprimary auditory cortex.

Differential adaptation to phonetic vs. spatial sound features presumably reflects local tuning properties of neuronal populations generating the N1 response (50). Single-unit recordings in animals have shown that auditory cortex neurons have a strong tendency to stimulus-specific adaptation (48, 49) as a function of the relative similarity of successive sounds. The fact that fMRI-weighted MEG activity in the posterior nonprimary auditory cortex was strongly adapted irrespective of phoneme changes suggests that the underlying neuronal populations are at best broadly tuned to phonetic features. The profound release from adaptation after sound-location changes in this posterior region, in turn, suggests that these neurons are sharply tuned to spatial features. Similarly, less adaptation after phoneme vs. sound-location changes in the anterior "what" areas of nonprimary auditory cortex suggests that neurons in this region are more sharply tuned to phonetic vs. spatial features of sounds. Notably, this differential "what" vs. "where" response adaptation occurred ≈100 ms after sound onset (see also refs. 11 and 50). Such millisecond-scale phenomena, as well as subtle peak-latency differences between the posterior "where" and anterior "what" pathways, are difficult to detect by using fMRI or positron emission tomography data alone, because such effects are essentially time-collapsed in hemodynamic and metabolic signals.

Previous neuroimaging studies have shown that selective attention enhances auditory cortex responses (14, 33–43). Our present MEG results extend these findings and shed light on the underlying neural mechanisms, showing that selective attention modulates response adaptation in the anterior "what" and posterior "where" pathways of nonprimary auditory cortex in a feature-specific fashion. To our knowledge, this has not been shown in humans before. Given the lack of significant selective attention effects on N1 responses elicited by Adaptors, we propose that attention may enhance the selectivity of neurons in the "what" and "where" streams of nonprimary auditory cortex. The enhanced selectivity could reflect direct modulation of receptive fields by attention, as recently suggested by single-cell recordings in behaving ferrets (47). Selective attention may thus be based on short-term plasticity of auditory cortex, increasing the neurons' selectivity for relevant information, instead of simple amplification of neuronal responses (proposed to govern attentional modulation of visual cortices) (46, 56). Such feature-specific modulation of neuronal receptive fields by selective attention may facilitate adjustment and calibration of the perceptual system based on the particular acoustic environment and task requirements.

Feature-specific effects on auditory cortex receptive fields appear to be difficult to characterize with slower neuroimaging measures, showing mainly general activity enhancements, evident in both present and previous fMRI (14, 33–37, 43) and positron emission tomography (38–40) data. Here, only a trend toward feature specificity of fMRI attention effects was observed in the posterior auditory cortex ROIs (see *Supporting Results*). However, the present fMRI paradigm was designed to support MEG source analysis (i.e., both spatially and phonetically differing sound pairs were presented between volume acquisitions), which may have reduced its sensitivity to feature-specific fMRI adaptation effects in the anterior vs. posterior auditory cortices. Further studies are needed to determine whether selective attention modulates the adaptation of auditory fMRI signals in a feature-specific fashion, analogous to the effects shown in the visual system (45). [Although not discussed in detail here, fMRI revealed significant attention effects in the prefrontal and parietal ROIs, consistent with previous observations (14, 34, 36, 39, 43) (see *Supporting Results* and Table 1).]

The spatial selective-attention effects were most prominent in the ECDs localized in the right posterior nonprimary auditory cortex (Figs. 4 and 5). Given that our sound stimuli originated from the right hemifield, this lateralization may seem contradictory to dichotic-listening results suggesting most pronounced spatial attention effects contralaterally to the ear stimulated (38, 42, 43). However, in a natural setting, auditory localization is based on binaural cues, simulated in the present study by using binaural room impulse responses (54). The fact that dichotic experiments apply monaural stimuli separately to each ear may overemphasize the contralateralization of auditory–spatial attention effects. Using binaural stimuli, the present evidence of dual pathways, *per se*, suggested that sound identity and location are processed bilaterally at the cortical level, consistent with earlier findings of bilateral auditory cortex activations to speech (31) and spatial sounds (29).

Presumably, the human auditory cortex "what" and "where" pathways interact closely to facilitate perception of auditory objects. Our MEG measurements show that the posterior

"where" stream is activated significantly earlier (≈30 ms in ECD models) than the anterior "what" stream. Interestingly, recent theories of visual recognition (57) suggest that the faster dorsal (i.e., "where") visual pathway may provide coarse "initial guesses" of object identity for the slower and more specific ventral (i.e., "what") pathway through bottom-up and top-down interactions. Analogously, the posterior auditory "where" pathway could accomplish rapid and coarse stimulus analysis required for shifting and maintaining attention to the features of a relevant auditory object (50), thus enabling the human brain to use top-down spatial information in auditory object perception. Based on psychophysical studies (58), such segregation mechanism could be particularly helpful in an environment with multiple physically overlapping sound sources (e.g., conversation in a crowded space).

In conclusion, our spatiotemporal brain imaging data demonstrate that processing of sound identity and location is implemented in parallel "what" and "where" pathways in the human nonprimary auditory cortex, supporting the view that different sensory systems process information by common principles (1, 3). Our results demonstrate an essential principle of top-down modulation of human auditory cortex by showing that feature-specific attention increases selectivity of neuronal populations for task-relevant information. The human auditory cortex can thus be modified, not only by previous experience but also in real time, to allow fine-tuning of local neuronal networks based on situational requirements. A dynamic neuronal architecture underlies our vital ability to concentrate on relevant auditory information in complex acoustic environments.

Methods

Subjects, Stimuli, and Tasks. During fMRI and MEG measurements, healthy right-handed (Edinburgh Test for Handedness) native Finnish speakers with normal hearing ($n = 9$; age, 21–44 years; three females) attended to either spatial or phonetic attributes of a sound sequence or ignored stimulation (Fig. 1 *a* and *b*). This sequence included pairs of Finnish vowels /æ/ and /ø/ (duration, 300 ms; 10-ms rise/fall times; intensity, 80-dB sound pressure level) simulated from straight ahead or 45° to the right (interpair interval, 3.4 s; gap between stimuli, 250 ms). 3D sounds were created by convolving raw vowel recordings with acoustic impulse responses measured at the ears of a manikin head (54). A horizontal 45° difference was selected to produce a location difference as equivalent as possible to the /æ/ vs. /ø/ phonetic category difference (see *Supporting Methods* in *Supporting Text*). There was a location difference, a phonetic difference, or no difference between the first stimulus of the pair (termed Adaptor) and the second stimulus of the pair (termed Probe). The subjects were instructed to press a button with the right index finger upon hearing two consecutive pairs identical with respect to the target attribute ($P = 0.13$). The target attribute, prompted with a visual cue, alternated in consecutive blocks (60-s Attend Location, 60-s Attend Phoneme, and 30-s Ignore conditions). In the Ignore condition, the subjects were instructed to rest (looking at a fixation mark) and ignore the stimuli. In the fMRI sessions the stimulus and task paradigms were otherwise identical, but all these blocks, and an additional rest condition with no stimuli, lasted for 30 s. Before sessions, subjects were trained until they switched the task correctly. In the task instructions, accuracy was emphasized more than the speed of performance.

Data Acquisition. Human subjects' approval was obtained and voluntary consents were signed before each measurement. MEG (306-channel; passband, 0.01–172 Hz; sampling rate, 600 Hz) (Elekta Neuromag, Helsinki, Finland) was measured in a magnetically shielded room. Two-second (200-ms baseline) epochs time-locked to onset of the sound pairs were averaged off-line (40-Hz lowpass; 1,024-point window). In a separate session, whole-head 3T fMRI (Siemens Trio, Erlangen, Germany) was recorded to obtain *a priori* knowledge of activated areas to guide cortically constrained MEG source analysis. To circumvent response contamination by scanner noise, a sparse-sampling gradient-echo BOLD sequence was used (TR/TE = 10,200/30 ms; flip angle, 90°; 20 axial 5-mm slices along the anterior–posterior commissure line; 0.5 mm gap; 3.1 × 3.1 mm in-plane), with the coolant pump switched off. Three sound pairs (similar to those used in MEG session; Fig. 1 *a* and *b*) were presented between the echoplanar imaging volume acquisitions ($n = 216$), starting 170 ms after the onset of the 8.5-s silent period and followed by a 950-ms gap between the last sound's offset and subsequent echoplanar imaging.

Data Analysis. ***Localizing "what" and "where" streams of auditory cortex.*** We used a 2-fold MEG source modeling approach to (*i*) localize the auditory cortex areas underlying "what" and "where" processing at N1 latency and (*ii*) investigate the hypothesized attentional modulation of response adaptation (see Fig. 1*c*) in the anterior and posterior auditory cortices.

To localize the dual pathways it was necessary to overcome the methodological compromises offered by fMRI or MEG alone. Therefore, the auditory cortex areas associated with "what" and "where" processing at the N1 latency were studied with fMRI-biased depth-weighted ℓ_2 minimum-norm estimates (55, 59) (see *Supporting Methods*). To combine functional data with information of the head anatomy, T1-weighted 3D MRI (TR/TE = 2,750/3.9 ms, 1.3 × 1×1.3 mm^3, 256 × 256 matrix) data were recorded separately, for individual boundary element models (55) and for reconstruction of cortical surface representations (60). This information was used in computing the MEG forward solutions. Current sources were confined within the cortical gray matter by using a loose orientation constraint. The minimum-norm estimates 90% weighted by significant fMRI activations ($P < 0.001$) in each source location were then calculated (59). Based on previous studies (59), the fMRI priors were based on a common weighting factor across the different stimulation conditions of the MEG analysis. That is, the fMRI weighting was based on activations pooled across the different attention–task conditions. To maximize the signal-to-noise ratio, the averaged MEG data were pooled across the attentional and Ignore conditions into three classes based on the within-pair similarity (Location Change, Phoneme Change, or Two Similar Sounds).

For group statistics, an anterior (anterolateral HG, extending to STG and PP) and a posterior (PT, posterior STG) ROI (on average ≈562 mm^2 of cortical surface) was individually selected in each hemisphere of each subject (Fig. 3) (see *Supporting Methods*). Given the large interindividual variability of the human auditory cortices (61), the ROIs were individually adjusted based on fMRI-weighted MEG activation patterns at the N1 peak latency. The average source activity was calculated from each ROI individually and then normalized within each ROI to a distribution with mean = 1 and SD = 1. A hemisphere by condition ANOVA with *a priori* contrasts (with Greenhouse–Geisser correction) tested the influence of sound changes on N1 adaptation in fMRI-weighted MEG data.

Quantifying selective attention effects in auditory cortex. Our second hypothesis was that selective attention to phonetic vs. spatial features differentially modulates adaptation in the anterior "what" vs. posterior "where" auditory pathways, respectively. Three subaverages of brain activity, corresponding to the three task instructions (Attend Location, Attend Phoneme, and Ignore; see Fig. 1 *a* and *b*), were calculated for the responses to each of the three sound-pair conditions (identical, spatially discordant, and phonetically discordant). To test our second hypothesis, we estimated the timing and amplitudes of anterior and posterior N1 subcomponents using an ECD approach analogous to previous studies (50, 53).

Although the ECD locations approximate the center of gravity of underlying neural activity (55), this approach is less sensitive to crosstalk (59) across different sources than distributed estimates (55), thus offering a robust model for contrasting attention-dependent modulations of the anterior and posterior auditory cortex N1 sources.

The N1 signals recorded from a subset of gradiometer channels (on average 40 per hemisphere) covering the left and right temporal lobes were used in the ECD modeling (55) (see *Supporting Methods*). The posterior N1 was fitted at the ascending phase (≈90 ms of the sound onset) and the anterior N1 was fitted at the descending phase (≈120 ms) of the N1 response to Adaptors (the goodness-of-fit was >80% for each ECD fitted). The resulting posterior and anterior ECDs (see *Supporting Results*) were then entered into a time-varying multidipole model to explain the recorded MEG responses. One multi-ECD estimate per hemisphere (based on the same channel selection across all conditions) was used to model each attentional condition in each subject. The attentional effects were tested by using an ANOVA with *a priori* contrasts (with Greenhouse–Geisser correction), including the following factors: serial position of stimuli (Adaptor vs. Probe), hemisphere, type of attention (Attend Location vs. Attend Phoneme vs. Ignore), dipole location (anterior vs. posterior), and type of stimulus change within a pair.

fMRI Analysis. After preprocessing, the fMRI time series were analyzed by using a general linear model (see *Supporting Methods*). Each subject's functional volumes were aligned with their anatomical images. The corresponding cortical surface representations were coregistered to a spherical standard space (60) for a surface-based random-effects model of group activations, calculated in addition to the individual activation maps used in the MEG source analysis. Six ROIs per hemisphere (anterior auditory cortex, posterior auditory cortex, posterior parietal, inferior frontal, dorsolateral prefrontal, and premotor) were selected based on the significant group activations (see Fig. 7, which is published as supporting information on the PNAS web site). The ROI activations, constrained by voxels showing significant individual activations ($P < 0.01$), were entered into a random-effects model to compare activations in different task conditions.

We thank Leonardo Angelone, Deirdre Foxe, Valerie Carr, Mark Halko, and Drs. Johanna Pekkola and Patrick Purdon for their help. This work was supported by National Institutes of Health Grants R01 HD040712, R01 NS037462, and P41 RR14075; the National Center for Research Resources; National Science Foundation Grant 0351442; the Mental Illness and Neuroscience Discovery (MIND) Institute; the American Heart Association; the Ella and Georg Ehrnrooth Foundation; the Emil Aaltonen Foundation; the Finnish Cultural Foundation; and Academy of Finland Grants 206368, 44897, and 213470.

1. Rauschecker JP, Tian B (2000) *Proc Natl Acad Sci USA* 97:11800–11806.
2. Tian B, Reser D, Durham A, Kustov A, Rauschecker JP (2001) *Science* 292:290–293.
3. Ungerleider L, Mishkin M (1982) in *Analysis of Visual Behavior*, eds Ingle D, Goodale M, Mansfield R (MIT Press, Cambridge, MA), pp 549–586.
4. Kastner S, Ungerleider LG (2000) *Annu Rev Neurosci* 23:315–341.
5. Clarke S, Bellmann A, De Ribaupierre F, Assal G (1996) *Neuropsychologia* 34:587–603.
6. Clarke S, Bellmann A, Meuli RA, Assal G, Steck AJ (2000) *Neuropsychologia* 38:797–807.
7. Clarke S, Bellmann Thiran A, Maeder P, Adriani M, Vernet O, Regli L, Cuisenaire O, Thiran JP (2002) *Exp Brain Res* 147:8–15.
8. Adriani M, Maeder P, Meuli R, Thiran AB, Frischknecht R, Villemure JG, Mayer J, Annoni JM, Bogousslavsky J, Fornari E, *et al.* (2003) *Exp Brain Res* 153:591–604.
9. Alain C, Arnott SR, Hevenor S, Graham S, Grady CL (2001) *Proc Natl Acad Sci USA* 98:12301–12306.
10. Arnott SR, Binns MA, Grady CL, Alain C (2004) *NeuroImage* 22:401–408.
11. De Santis L, Clarke S, Murray MM (2006) *Cereb Cortex*, in press.
12. Bushara KO, Weeks RA, Ishii K, Catalan MJ, Tian B, Rauschecker JP, Hallett M (1999) *Nat Neurosci* 2:759–766.
13. Rämä P, Poremba A, Sala JB, Yee L, Malloy M, Mishkin M, Courtney SM (2004) *Cereb Cortex* 14:768–780.
14. Rämä P, Courtney SM (2005) *NeuroImage* 24:224–234.
15. Weeks RA, Aziz-Sultan A, Bushara KO, Tian B, Wessinger CM, Dang N, Rauschecker JP, Hallett M (1999) *Neurosci Lett* 262:155–158.
16. Maeder PP, Meuli RA, Adriani M, Bellmann A, Fornari E, Thiran JP, Pittet A, Clarke S (2001) *NeuroImage* 14:802–816.
17. Kaiser J, Lutzenberger W (2001) *NeuroReport* 12:3479–3482.
18. Kaiser J, Ripper B, Birbaumer N, Lutzenberger W (2003) *NeuroImage* 20:816–827.
19. Arnott SR, Grady CL, Hevenor SJ, Graham S, Alain C (2005) *J Cognit Neurosci* 17:819–831.
20. Murray MM, Camen C, Gonzalez Andino SL, Bovet P, Clarke S (2006) *J Neurosci* 26:1293–1302.
21. Brunetti M, Belardinelli P, Caulo M, Del Gratta C, Della Penna S, Ferretti A, Lucci G, Moretti A, Pizzella V, Tartaro A, *et al.* (2005) *Hum Brain Mapp* 26:251–261.
22. Krumbholz K, Schonwiesner M, von Cramon DY, Rubsamen R, Shah NJ, Zilles K, Fink GR (2005) *Cereb Cortex* 15:317–324.
23. Tata MS, Ward LM (2005) *Exp Brain Res* 167:481–486.
24. Tata MS, Ward LM (2005) *Neuropsychologia* 43:509–516.
25. Warren JD, Zielinski BA, Green GG, Rauschecker JP, Griffiths TD (2002) *Neuron* 34:139–148.
26. Zimmer U, Macaluso E (2005) *Neuron* 47:893–905.
27. Binder JR, Frost JA, Hammeke TA, Bellgowan PS, Springer JA, Kaufman JN, Possing ET (2000) *Cereb Cortex* 10:512–528.
28. Obleser J, Boecker H, Drzezga A, Haslinger B, Hennenlotter A, Roettinger M, Eulitz C, Rauschecker JP (2006) *Hum Brain Mapp* 27:562–571.
29. Warren JD, Griffiths TD (2003) *J Neurosci* 23:5799–5804.
30. Griffiths TD, Warren JD (2002) *Trends Neurosci* 25:348–353.
31. Zatorre RJ, Evans AC, Meyer E, Gjedde A (1992) *Science* 256:846–849.
32. Belin P, Zatorre RJ (2000) *Nat Neurosci* 3:965–966.
33. Grady CL, Van Meter JW, Maisog JM, Pietrini P, Krasuski J, Rauschecker JP (1997) *NeuroReport* 8:2511–2516.
34. Jäncke L, Shah NJ, Posse S, Grosse-Ryuken M, Muller-Gartner HW (1998) *Neuropsychologia* 36:875–883.
35. Jäncke L, Mirzazade S, Shah NJ (1999) *Neurosci Lett* 266:125–128.
36. Jäncke L, Shah NJ (2002) *Neurology* 58:736–743.
37. Petkov CI, Kang X, Alho K, Bertrand O, Yund EW, Woods DL (2004) *Nat Neurosci* 7:658–663.
38. Alho K, Vorobyev VA, Medvedev SV, Pakhomov SV, Roudas MS, Tervaniemi M, van Zuijen T, Näätänen R (2003) *Brain Res Cognit Brain Res* 17:201–211.
39. Zatorre RJ, Mondor TA, Evans AC (1999) *NeuroImage* 10:544–554.
40. Hugdahl K, Bronnick K, Kyllingsbaek S, Law I, Gade A, Paulson OB (1999) *Neuropsychologia* 37:431–440.
41. Hillyard S, Hink R, Schwent V, Picton T (1973) *Science* 182:177–180.
42. Woldorff MG, Gallen CC, Hampson SA, Hillyard SA, Pantev C, Sobel D, Bloom FE (1993) *Proc Natl Acad Sci USA* 90:8722–8726.
43. Jäncke L, Buchanan TW, Lutz K, Shah NJ (2001) *Brain Lang* 78:349–363.
44. Reynolds JH, Desimone R (2003) *Neuron* 37:853–863.
45. Murray SO, Wojciulik E (2004) *Nat Neurosci* 7:70–74.
46. Hillyard SA, Vogel EK, Luck SJ (1998) *Philos Trans R Soc London B* 353:1257–1270.
47. Fritz J, Shamma S, Elhilali M, Klein D (2003) *Nat Neurosci* 6:1216–1223.
48. Ulanovsky N, Las L, Nelken I (2003) *Nat Neurosci* 6:391–398.
49. Nelken I, Fishbach A, Las L, Ulanovsky N, Farkas D (2003) *Biol Cybern* 89:397–406.
50. Jääskeläinen IP, Ahveninen J, Bonmassar G, Dale AM, Ilmoniemi RJ, Levänen S, Lin FH, May P, Melcher J, Stufflebeam S, *et al.* (2004) *Proc Natl Acad Sci USA* 101:6809–6814.
51. Näätänen R, Sams M, Alho K, Paavilainen P, Reinikainen K, Sokolov EN (1988) *Electroencephalogr Clin Neurophysiol* 69:523–531.
52. Lu ZL, Williamson SJ, Kaufman L (1992) *Science* 258:1668–1670.
53. Sams M, Hari R, Rif J, Knuutila J (1993) *J Cognit Neurosci* 5:363–370.
54. Shinn-Cunningham BG, Kopco N, Martin TJ (2005) *J Acoust Soc Am* 117:3100–3115.
55. Hämäläinen M, Hari R, Ilmoniemi R, Knuutila J, Lounasmaa O (1993) *Rev Mod Phys* 65:413–497.
56. Treue S, Martinez Trujillo JC (1999) *Nature* 399:575–579.
57. Bar M, Kassam KS, Ghuman AS, Boshyan J, Schmidt AM, Dale AM, Hämäläinen MS, Marinkovic K, Schacter DL, Rosen BR, *et al.* (2006) *Proc Natl Acad Sci USA* 103:449–454.
58. Durlach NI, Mason CR, Shinn-Cunningham BG, Arbogast TL, Colburn HS, Kidd G Jr (2003) *J Acoust Soc Am* 114:368–379.
59. Dale A, Liu A, Fischl B, Buckner R, Belliveau J, Lewine J, Halgren E (2000) *Neuron* 26:55–67.
60. Fischl B, Sereno MI, Tootell RB, Dale AM (1999) *Hum Brain Mapp* 8:272–284.
61. Rademacher J, Morosan P, Schormann T, Schleicher A, Werner C, Freund HJ, Zilles K (2001) *NeuroImage* 13:669–683.