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## Differential brain activation patterns during perception of voice and tone onset time series: a MEG study

Andrew C. Papanicolaou,<sup>a,\*</sup> Eduardo Castillo,<sup>a</sup> Joshua I. Breier,<sup>a</sup> Robert N. Davis,<sup>a,b</sup>  
Panagiotis G. Simos,<sup>a</sup> and Randy L. Diehl<sup>c</sup>

<sup>a</sup> Vivian L. Smith Center for Neurologic Research, Department of Neurosurgery, University of Texas—Houston Medical School, Houston, TX 77030, USA

<sup>b</sup> Department of Psychology, University of Houston, Houston, TX, USA

<sup>c</sup> Department of Psychology, University of Texas at Austin, Austin, TX, USA

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### Abstract

Evoked magnetic fields were recorded from 18 adult volunteers using magnetoencephalography (MEG) during perception of speech stimuli (the endpoints of a voice onset time (VOT) series ranging from /ga/ to /ka/), analogous nonspeech stimuli (the endpoints of a two-tone series varying in relative tone onset time (TOT), and a set of harmonically complex tones varying in pitch. During the early time window (~60 to ~130 ms post-stimulus onset), activation of the primary auditory cortex was bilaterally equal in strength for all three tasks. During the middle (~130 to 800 ms) and late (800 to 1400 ms) time windows of the VOT task, activation of the posterior portion of the superior temporal gyrus (STGp) was greater in the left hemisphere than in the right hemisphere, in both group and individual data. These asymmetries were not evident in response to the nonspeech stimuli. Hemispheric asymmetries in a measure of neurophysiological activity in STGp, which includes the supratemporal plane and cortex inside the superior temporal sulcus, may reflect a specialization of association auditory cortex in the left hemisphere for processing speech sounds. Differences in late activation patterns potentially reflect the operation of a postperceptual process (e.g., rehearsal in working memory) that is restricted to speech stimuli.

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The contributions of the posterior portion of the left temporal lobe (especially Brodmann's area 22) to language comprehension have been known at least since the time of Karl Wernicke. Following Wernicke's (1874) seminal publication, numerous reports on the effects of focal lesions have confirmed the early findings (e.g., Damasio, 1998). Further confirmation of the role of Wernicke's area in language comprehension has been obtained during the last decade with functional brain imaging studies using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) (Binder et al., 1997; Demonet et al.,

1993; Fiez et al., 1996; Petersen et al., 1988; Raichle, 1994). More recent imaging studies using magnetoencephalography (MEG) have shown that the posterior portion of the left superior temporal gyrus (STGp), which comprises the largest portion of Wernicke's area, is necessary for phonological analysis of speech sounds, whereas both STGp and the middle temporal gyrus are activated when a task requires semantic in addition to phonological processing of spoken or printed words. This evidence (Breier et al., 1999a; Castillo et al., 2001; Simos et al., 1998, 1999, 2000a, 2002), collected noninvasively from normal adults and children, was further strengthened by the results of a direct cortical stimulation study involving four patients (Simos et al., 2000b). Other studies that examined the speech perception abilities of patients with left posterior temporal lesions (Blumstein et al., 1977) and the effects of electrocortical interference in this region (Boatman et al., 1995) corroborate these findings. More recent reports, however, present

\* Corresponding author: Division of Clinical Neurosciences, Department of Neurosurgery, University of Texas—Houston Health Science Center, 6431 Fannin Street, Suite 7.152, Houston, TX 77030, USA. Fax: +1-713-500-7787.

E-mail address: [Andrew.C.Papanicolaou@uth.tmc.edu](mailto:Andrew.C.Papanicolaou@uth.tmc.edu) (A.C. Papanicolaou).

contradictory results suggesting that the brain circuit specialized for speech perception may not rely exclusively on left posterior temporal lobe structures but may also comprise homologous regions in the right hemisphere (for a review see Hickok and Poeppel, 2000).

Although the above findings clearly implicate STGp as being critical for the phonological analysis of speech sounds, it remains unclear from imaging results whether this region is also critically involved in lower-level analysis of speech stimuli, which presumably involves extraction of perceptually relevant cues (phonetic analysis). It is also unclear whether the role of this region is restricted to the analysis of speech stimuli or whether it extends also to the analysis of nonspeech sounds having comparable acoustic complexity. The notion of a specialized perceptual mechanism for speech sounds has been advocated for many years (Liberman, 1996; Liberman et al., 1967; Liberman and Mattingly, 1985; Studdert-Kennedy and Shankweiler, 1970), and STGp is a plausible cortical substrate for such a mechanism. Alternatively, STGp may be critical for the analysis of certain complex acoustic stimuli, regardless of whether such stimuli are perceived as speech sounds or not. In other words, it is possible to create nonspeech stimuli that contain acoustic cues similar to those used by listeners to discriminate speech sounds. Along these lines, a specialization of the left STGp has been suggested for analyzing rapid temporal cues regardless of whether they are embedded in a speech context or not (Liegeois-Chauvel et al., 1999; Nicholls, 1996; Robin et al., 1990).

Early studies regarding hemispheric specialization for speech perception using dichotic listening techniques found that subjects exhibited a right ear advantage, indicative of greater left hemisphere processing, for most speech stimuli (Bradshaw and Nettleton, 1981; Bryden, 1982; Cutting, 1974). However, a right ear advantage was also observed for the identification of certain nonspeech stimuli, including square-wave segments differing in rise time (Blechner, 1976) and temporal order judgments of multiple brief sounds differing in pitch or duration (Halperin et al., 1973). In contrast, perception of various other types of nonspeech sounds, such as isolated formant transitions (Blechner, 1977) or sine-wave analogs of consonant–vowel syllables (Cutting, 1974), showed either a left-ear advantage or no ear advantage. Thus, the evidence from dichotic listening experiments is equivocal with respect to the possible specialized role of the left hemisphere in the processing of nonspeech sounds. Such stimuli might be processed by the same mechanism that handles speech sounds or, alternatively, processed bilaterally, even by the right hemisphere.

In the present study, we used MEG to record brain activity of individual participants engaged in discriminating (a) consonant–vowel syllables varying along the voice onset time (VOT) dimension, (b) nonspeech two-tone patterns of the same duration and intensity as the speech sounds and varying along a relative tone onset time (TOT) dimension, and (c) harmonically complex tones varying in pitch. Given

that MEG can, in principle, provide an outline of regionally elevated levels of neurophysiological activity in real time, it is well-suited to examine whether bilaterally symmetric activation reported by several fMRI and PET studies (e.g., Belin et al., 2002; Jäncke et al., 2002) is a by-product of the prolonged signal integration time necessary to capture task-related hemodynamic responses.

Our choice of VOT and TOT stimuli was motivated by two considerations. First, we wanted to use a series of nonspeech stimuli that are acoustically analogous to the speech stimulus series, at least with respect to the primary (within-series) dimension of variation. For the stimulus ranges used here, the VOT and TOT items may each be described as consisting of a high- and a low-frequency component, or spectral band, such that the onset of the low-frequency component or band is delayed by some interval (ranging from 0 to 60 ms) relative to the onset of the high-frequency band. To this extent, then, both the VOT and TOT stimulus series are acoustically comparable. Second, although VOT (/ga-/ka/) stimuli sound very different from TOT stimuli, there are interesting similarities in how human listeners identify and discriminate members of the two sets. Lisker and Abramson (1970); Abramson and Lisker, 1970) showed that listeners perceive VOT stimuli *categorically*. That is, their phoneme labeling performance yielded relatively sharp category boundaries, and their ability to discriminate between adjacent stimuli along the VOT dimension was near chance within a phoneme category, but near perfect when a stimulus pair straddled a phoneme boundary. Pisoni (1977) reported quite similar categorical labeling and discrimination functions for TOT stimuli that shared the relative temporal onset properties of the VOT stimuli used by Lisker and Abramson (1970). This parallel between speech and nonspeech results suggests that there may be common mechanisms involved in the processing of VOT and TOT stimuli. For example, Pisoni posited the existence of a common mechanism that discriminates (or fails to discriminate) differences in temporal order of component events at stimulus onset (see also Miller et al., 1976). A third set of stimuli, consisting of harmonically complex tones varying in fundamental frequency, were included in the design of the present study. Like the TOT series, these stimuli were not perceived as speech sounds but, unlike the two-tone TOT sounds, they did not contain any temporal or spectral cues that could support discrimination in a categorical fashion. Such stimuli are typically associated with bilaterally symmetric or predominantly right superior temporal lobe activation (Griffiths, 2001; Zatorre, 1988).

To understand the process by which brain activation maps were constructed for each task, a brief introduction to the MEG procedures may be useful. MEG is a completely noninvasive method of functional brain imaging, akin to quantitative electroencephalography. It consists first of recording, on the head surface, magnetic flux associated with electrical currents in activated sets of neurons (Lewine, 1990; Papanicolaou, 1998; Papanicolaou and Tarkka,

1996). Second, it consists of estimating the location of such sets or activity sources. Third, the method involves projecting the sources onto a structural magnetic resonance image of the brain allowing for visualization of the activated brain regions. MEG has undergone a rapid evolution during the past few years and is used by an increasing large number of centers for mapping the primary sensory cortex (Nakasato et al., 1997; Ruohonen et al., 1996; Seki et al., 1996; Sobel et al., 1993), as well as association cortex (Rogers et al., 1991, 1993; Simos et al., 1997).

The procedures for imaging the brain mechanisms of sensory and cognitive functions through MEG can be summarized as follows. Stimuli evoke brain activity soon after they impinge on the sensory receptors. One basic aspect of such activity is the intra- and extracellular flow of ions, which generate electrical currents and magnetic fields. Repetitive application of the stimulus results in repeated evocation of the same currents and fields which, when recorded on the head surface, result in the well-known evoked potentials (EPs) and their magnetic counterparts, the evoked fields (EFs). The distribution of EFs on the head surface lends itself, much more readily than the distribution of EPs, to mathematical estimates of the location and extent of brain activation sources.

EFs, no less than the familiar evoked potentials, are waveforms representing variations of brain activity over time following stimulus presentation. Some of these variations are observed consistently across various experimental conditions and are referred to as components. There are two basic types of components: early ones like the N1 (and its magnetic counterpart N1m) that have been shown to reflect activation of primary sensory cortex (Nakasato et al., 1997; Ruohonen et al., 1996; Seki et al., 1996; Sobel et al., 1993), and those that occur later in time that reflect activation of association cortex (Rogers et al., 1991, 1993; Simos et al., 1997). On the basis of the early components, one can construct images of the brain mechanisms of sensory functions, whereas the late ones are used for constructing maps of higher functions such as language.

In a series of studies involving more than 200 individuals thus far, we have established the spatiotemporal pattern of brain activation specific to simple somatosensory functions, aural language comprehension, and word reading, and have verified their stability or reproducibility over time (Breier et al., 1999b, 2000). Moreover, in a series of investigations still in progress (Papanicolaou et al., 1999; Simos et al., 1999), the validity and topographical specificity of these maps have been established by comparing them with the results of direct cortical stimulation mapping, and with the results of the intracarotid amytal (Wada) procedure in more than 60 adult patients and 20 children (see Breier et al., 1999c, 2001; Maestu et al., 2002, for initial reports on these patients). Having thus established the validity and the reliability of MEG mapping, we applied it in the present experiment to test three main predictions based on earlier results reviewed above. We expected that the early EF

components reflecting early auditory processing of the VOT, TOT, and complex tone stimuli would be localized in the primary auditory cortex and would be essentially bilaterally equal in strength. We also expected that for the VOT stimuli, the middle (measured between ~130 and 800 ms after stimulus onset) and late (observed between 800 and 1400 ms) EF components would reflect predominant activation of left hemisphere regions, primarily of the left STGp. Finally, we expected that the degree of posterior temporal lobe activation in response to the complex tone stimuli would be, on average, bilaterally symmetric or show a slight right hemisphere advantage (Griffiths, 2001; Zatorre, 1988) and that the degree of left STGp activation in particular would be lower in response to complex tone stimuli than to the speech syllables. In addition to testing these predictions, we explored the issue of whether the middle and late EF components for the TOT stimuli would also show a predominant activation of the left STGp, or a more bilateral activation pattern, or even greater activation of the right STGp.

## Materials and methods

### *Participants*

Eighteen adult normal volunteers (11 males, 7 females) participated in the study and were paid for their participation. The participants had a mean age of 31.11 years ( $SD = 7.78$ ) and ranged in age from 21 to 45 years. All participants had normal hearing. They participated in two separate experimental sessions involving the VOT, TOT, and complex tone tasks, which were given in a different random order to each participant. In one session, only behavioral responses were recorded; in the other session, brain activity was recorded.

### *Stimuli and procedures*

Seven consonant–vowel tokens that formed a velar voicing series with VOT values ranging from 0 to 60 ms in 10-ms steps served as stimuli in the VOT task. The syllables were prepared using the cascade branch of the Klatt88 software synthesizer. Variation of VOT was achieved by broadening the bandwidth of F1 and exciting F2 and F3 with a noise source during the period between stimulus onset and voicing source onset. The fundamental frequency (F0) was constant at 120 Hz for all syllables. The nominal formant frequencies at stimulus onset were 300, 1840, and 1960 Hz and changed linearly across a 55-ms transition period to 768, 1333, and 2522 Hz. The transitions were followed by a 200-ms steady-state segment resulting in a total stimulus length of 255 ms. In addition, the relative balance of low-frequency energy in the voicing source was enhanced by setting the spectral tilt parameter of the Klatt synthesizer to 10 along the entire length of the syllable. Finally, the voiced portions of the stimuli were low-pass filtered at 3200 Hz.

In the TOT task, stimuli were seven two-tone tokens, constructed according to the parameters described by Pisoni (1977). The TOT, or delay in the onset of the lower (500 Hz) tone in relation to the higher tone (1500 Hz), varied between 0 and 60 ms in 10-ms steps. The termination of the two tones occurred simultaneously. The duration of the 1500-Hz tone was always 230 ms. Seven two-tone sounds, modeled after the 0-ms TOT token, served as stimuli in the third task. The two tones started and ended simultaneously (with a total duration of 230 ms), but their frequency varied in equal steps, producing a change in pitch. The frequencies of the lower and higher tones for each of the seven sounds were as follows: 500/1500 Hz (lowest pitch), 530/1600 Hz, 560/1700 Hz, 590/1800 Hz, 620/1900 Hz, 650/2000 Hz, 680/2100 Hz (highest pitch).

In all three tasks, the stimuli were presented binaurally in pairs with an onset-to-onset interval of 2 s between pair members. The second stimulus could be any of the seven items of the respective series. During the MEG recordings, the subjects were asked to decide if the two tokens in each pair were the same or different, responding by raising their right (or left) index finger if the tokens were the same. The responding hand was counterbalanced across subjects. The interval between stimulus pairs was varied randomly across trials between 3 and 4 s. Stimulus delivery was accomplished via two 5-m-long plastic tubes terminating in ear inserts. Stimulus intensity was 80 dB SPL at the subject's outer ear. EFs were recorded to the first stimulus of each pair to ensure that the brain activity recorded corresponded to perceptual analysis operations, and did not reflect the additional cognitive operations that matching of the stimuli entails. The first stimulus in every pair was always a token from either endpoint of the VOT, TOT, or complex tone series, i.e., either a /ga/ with a 0-ms VOT or a /ka/ with a +60 ms VOT in the VOT task, a token with either a 0-ms or a +60-ms TOT in the TOT task, and either a lowest- or highest-pitch tone for the complex tone task. In this manner brain activity was always recorded in response to perceptually unambiguous stimuli.

MEG recordings were conducted with a whole-head, 148-channel neuromagnetometer array (4-D Neuroimaging, Magnes WH 2500) housed in a magnetically shielded chamber. The magnetic flux measurements were filtered with a bandpass filter between 0.1 and 50 Hz and digitized at 250 Hz. Intrinsic noise in each channel was  $< 10$  fT/Hz. To further reduce the amount of magnetic noise produced by remote sources, the MEG data were submitted to an interactive noise reduction procedure that aided in reducing environmental noise and is part of the signal analysis software. This procedure uses the magnetic flux recordings obtained on-line from 11 "reference sensors" (six magnetometers, and five first-order axial gradiometers) located at a distance of approximately 30 cm above the array of 148 magnetometers. The distance between these reference sensors and the intracranial generators of magnetic flux ensures that they record only "extraneous" flux (i.e., flux that is not

due to neuronal currents). Following each recording session the magnetic flux values recorded at each time point within each epoch were partialled out from the corresponding magnetic flux values measured by each of the 148 magnetometers. The single-trial EF segments in response to 70–80 stimulus presentations were averaged separately for each sensor after excluding those containing eye movement (as indicated by a peak-to-peak amplitude in the electro-oculogram in excess of  $50 \mu\text{V}$ ) or other myogenic or mechanical artifacts. Finally, the averaged epochs were digitally filtered with a low-pass filter of 20 Hz to improve signal quality and adjusted relative to the mean amplitude in the 150-ms pre-stimulus period to remove dc offset.

The intracranial generators of the observed EFs at successive 4-ms intervals were modeled as equivalent current dipoles (ECDs) by using the nonlinear Levenberg–Marquardt algorithm on a spherical head model. This method searched for the ECD that was most likely to have produced the observed magnetic field distribution at a given point in time (according to the Biot–Savart law). ECD solutions were considered as satisfactory on meeting two criteria: (1) a correlation coefficient of at least 0.90 between the observed and "best" predicted magnetic field distributions, and (2) a 95% confidence volume of  $30 \text{ cm}^3$  or smaller. The latter corresponded to the region that was most likely (i.e., in 95% of all possible repetitions of the measurement) to contain the source of the observed magnetic field distribution. The dipole fitting algorithm was applied to the magnetic flux measurements obtained from a group of 34–38 sensors, always including both magnetic flux extrema. ECD location was computed in reference to a Cartesian coordinate system defined by a set of three anatomical landmarks (fiducial points): the right and left external meati and the nasion. The line passing through the right and left external meati served as the *Y* axis. The line between the nasion and the midpoint of the *Y* axis defined the *X* axis, and the line perpendicular to the *X–Y* plane, passing through the intersection of the *X* and *Y* axes, defined the *Z* axis. The position of the magnetometers relative to the subject's head was precisely determined using five coils, three of which were attached to the fiducial points and two on the forehead. The coils were turned on briefly at the beginning and again at the end of the recording session, and their precise location in three-dimensional space was determined using a localization algorithm. During the recording session a fiberoptic motion detector was used to ensure that the subject did not change position relative to the sensor.

The degree of activation of a particular area, or the total duration of its activation, was estimated by the total number of successive dipoles that accounted for the EF components. Several studies from our group and others (Breier et al., 1999c, 2001; Papanicolaou et al., 1999; Simos et al., 1998a, 1999; Maestu et al., 2002) have provided evidence that the procedure for constructing brain activation profiles used in the present study is sufficiently accurate for identifying: (1) the hemisphere that is more prominently involved in

basic linguistic functions, and (2) specific regions within the dominant hemisphere that are indispensable for particular processes such as decoding and encoding of auditory and printed words. The results of these studies directly support the concurrent validity of our approach to deriving activation maps. The construct validity of the measure of brain activation used in this procedure reflects the degree to which the measure provides an accurate representation of both the spatial and temporal extent of regionally elevated levels of neurophysiological activity. The rationale for using the number of sequential activity sources as a dependent measure is based on the premise that processing of an incoming auditory stimulus requires a transient increase in neuronal signaling in one or more neuronal populations. This in turn produces a time-limited increase in intracellular currents which, once integrated, can be represented as an electrical dipole. The strength of the dipole (i.e., the magnitude of intracellular current) at each point in time is directly related to the strength of the resulting magnetic flux. The dipolar nature of the source can be ascertained from the dipolar appearance of the surface distribution of recorded magnetic flux (contour map). Assuming the presence of a dipolar source, the degree of confidence with which the underlying source is estimated by the dipole fitting program directly reflects the strength of the recorded magnetic flux at that point in time. (The correlation coefficient between the observed and an ideal or hypothesized underlying source is a widely used index of the degree to which the computed source solution approximates that of a dipolar source.) The number of activity source solutions that exceed a particular—empirically defined criterion—reflects the amount of time that the rate of neuronal signaling in a particular patch of cortex produces a detectable extracranial signature. This is a simplified account, as other factors also contribute to the strength of the recorded magnetic flux, such as the orientation of the cortical patch containing the active neurons relative to the plane of each magnetometer sensor and the characteristics of background noise, or magnetic flux produced by sources not related to the neurophysiological activity that processing of the stimuli entails. The empirically established concurrent validity of this measure, however, lends credence to the plausibility of the claim that the duration of focal cortical activity may be used as a measure of the “degree of engagement” of a particular cortical region in a given task. This measure complements similar measures employed by other imaging modalities, such as the spatial extent of cortex that shows differential hemodynamic modulation across two different tasks.

## Results

Judgment accuracy for all three series was more than 90% for all participants. As expected, all stimuli resulted in EFs with typical early and late components (see Fig. 1). The early portion of the EF is dominated by the N1m compo-

nent. As expected there was some variation in the onset, peak, and offset latency of the N1m component among participants. Corresponding mean, standard deviation, and range values for the VOT stimuli were for the onset,  $53 \pm 3.3$  (50–58) ms; for the peak,  $92 \pm 1.5$  (85–95) ms; and for the offset,  $132 \pm 4.9$  (128–140) ms. Corresponding values for the TOT stimuli were for the onset,  $54 \pm 2.8$  (51–60) ms; for the peak,  $87 \pm 1.8$  (82–92) ms; and for the offset,  $136 \pm 5.2$  (128–145) ms. The mean, standard deviation, and range for the complex tone stimuli were  $52 \pm 2.6$  (51–60) ms (onset),  $86 \pm 2.0$  (79–89) ms (peak), and  $125 \pm 4.4$  (123–140) ms (offset). The sources of the N1m component to VOT, TOT, and complex tone stimuli were distributed bilaterally on the floor of the Sylvian fissure, corresponding to the primary auditory cortex, where they have repeatedly been found in previous studies (e.g., Nakasato et al., 1997; Pantev and Lütkenhöner, 2000; Zouridakis et al., 1998). Average root mean square (RMS) values for the N1m component, which serve as an index of field strength, were 97 fT (left hemisphere) and 103 fT (right hemisphere) in response to the speech stimuli, 142 fT (left hemisphere) and 144 fT (right hemisphere) in response to the two-tone stimuli, and 115 fT (left hemisphere) and 125 fT (right hemisphere) in response to the complex tone stimuli. A series of ANOVAs with Task and Hemisphere as within-subject factors performed on the latency and RMS values revealed a main effect of Task for RMS,  $F(2, 34) = 6.40$ ,  $P < 0.004$ . Post hoc tests indicated that magnetic flux amplitude was greater in response to the TOT series than in response to the VOT series,  $t(1,17) = 2.74$ ,  $P < 0.014$ .

The sources of the late EF components, computed after the expiration of the N1m component and up to 1400 ms post-stimulus onset, were localized not only in STG as anticipated, but also, though in far smaller concentrations, in the adjacent middle temporal gyrus, supramarginal gyrus, and mesial temporal cortex. Because of the lack of consistent activation in these other areas, and as we were specifically interested in interhemispheric asymmetries in activity occurring in the primary and surrounding association auditory cortex, we restricted analyses to the posterior portion of STG. This region was defined as the area extending rostrocaudally from the middle of the temporal lobe up to, and including, the temporoparietal junction, and dorsoventrally from the temporal plane and lower bank of the Sylvian fissure to the fundus of the superior temporal sulcus (STS). To investigate the temporal variation of activity across the various components, we further divided the portion of the EF after the expiration of the N1m component (which occurred on average at approximately 130 ms) into a middle time window (~130–800 ms) and a late time window (800–1400 ms). The mean number of activity sources per participant during each of the three time windows (early, middle, late) is presented for each hemisphere in Fig. 2.

The spatiotemporal profile of activity in STGp was examined using an ANOVA with Hemisphere (left, right),

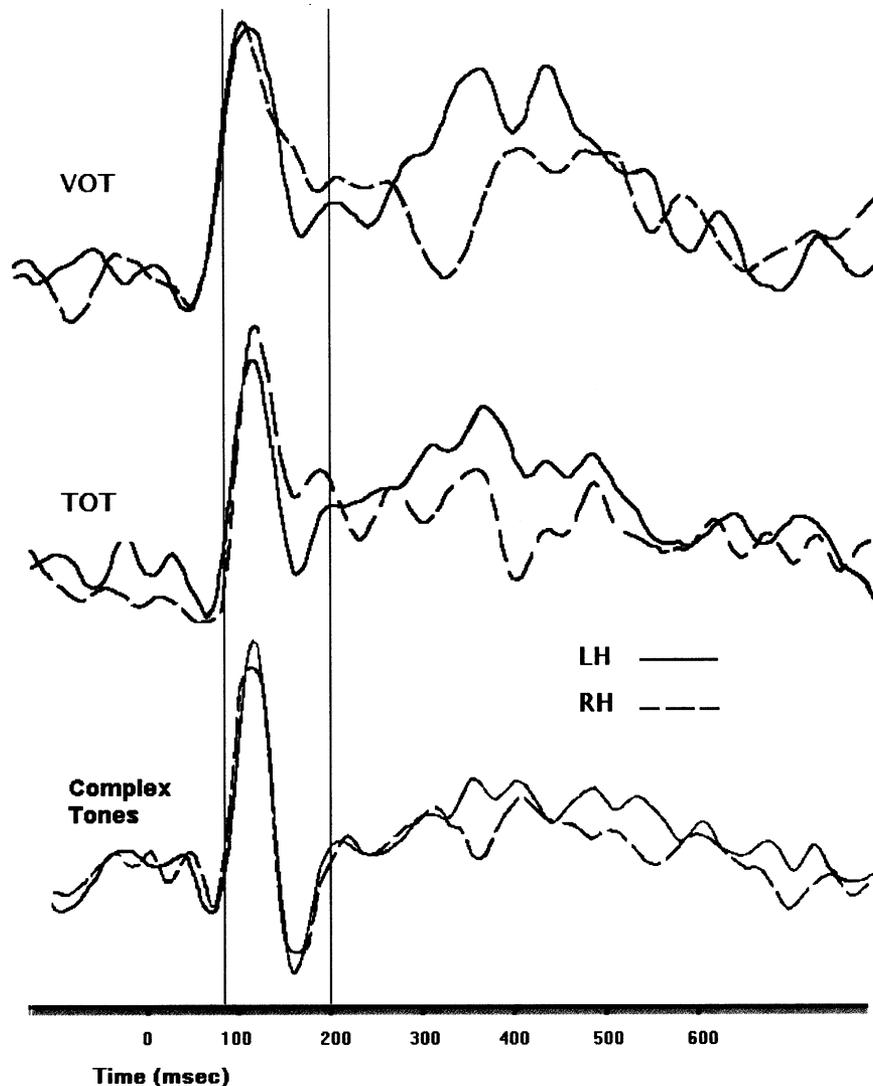


Fig. 1. Sample EF waveforms to (top) VOT, (middle) TOT, and (bottom) complex tone stimuli from the left hemisphere maximum (solid line) and the right hemisphere maximum (dashed line), showing the similarity of the N1m component over both hemispheres. Sensors were located symmetrically over the left and right posterior temporal areas. Note that the stimulus is presented at time zero.

Task (VOT, TOT, complex tones), and Time Window (early, middle and late) as within-subject factors. There was a significant three-way interaction (Hemisphere  $\times$  Task  $\times$  Time),  $F(4, 68) = 2.94$ ,  $P < 0.035$ , indicating that differences in interhemispheric asymmetries in activation for the speech and nonspeech tasks differed across tasks and time windows. Follow-up analyses within each time window were treated as a family, using a critical value of  $P < 0.016$  to maintain family-wise Type I error at  $< 0.05$  for each ANOVA. There were significant Task  $\times$  Hemisphere interactions for both the middle,  $F(2, 34) = 5.30$ ,  $P < 0.014$ , and late,  $F(2, 34) = 4.70$ ,  $P < 0.016$ , time windows. Pairwise contrasts were treated as a family within each time window. Based on the Bonferroni method for a total of nine comparisons, the  $\alpha$  level was set at 0.006. For the middle time window the only significant effect reflected greater left over right STGp activation in response to the speech stimuli,

$t(1,17) = 6.85$ ,  $P < 0.0001$ .  $P$  values for all other contrasts were  $> 0.1$  with the exception of a trend toward a greater number of activity sources in response to speech than in response to complex tone stimuli in the left STGp,  $t(1,17) = 3.10$ ,  $P < 0.007$ . A predominance of left over right STGp in the number of activity sources was also found for the late window in the VOT task,  $t(1,17) = 3.79$ ,  $P < 0.001$ , with only a trend for greater activity in response to speech than in response to two-tone stimuli in the left STGp,  $t(1,17) = 2.43$ ,  $P < 0.026$ .

As shown in Fig. 2, approximately twice as many activity sources were found in the left than in the right STGp during the middle window in response to the VOT series (100% difference). In contrast, left STGp activity was only 40% greater than activity in the right STGp for the TOT stimuli and just 4% greater than the right STGp in response to complex tone stimuli. During the late time window the

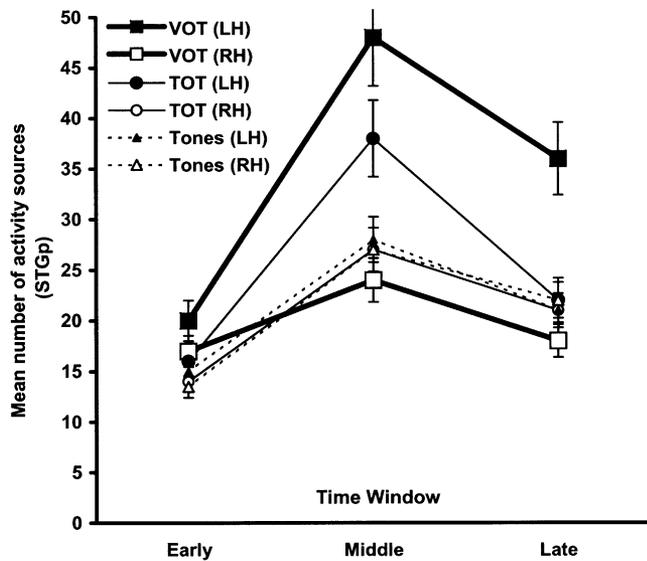


Fig. 2. Number of intracranial sources that account for the early (0 to ~130 ms), middle (~130 to 800 ms), and late (800 to 1400 ms) time windows as a function of task (VOT, thick lines; TOT, thin lines; complex tones, dotted lines) and hemisphere (LH, filled markers; RH, open markers). Error bars represent SEM.

percentage difference between left and right STGp was 100% in the VOT task, 5% in the TOT task, and -4.5% in the complex tone task.

The distribution of individual scores supported the group data. Laterality indices were computed to describe hemispheric asymmetries in the number of activity sources in STGp, using the formula  $(L-STGp - R-STGp) / (L-STGp + R-STGp)$ . Consistent, left-leaning asymmetries were found only during the VOT task for both the middle (17 of 18 participants, binomial test:  $P < 0.0001$ ) and late (15 of 18 participants, binomial test:  $P < 0.008$ ) time windows. A nonsignificant majority of participants showed a similar trend during the middle time window in the TOT task (12/18,  $P > 0.24$ ). This trend was reversed during the late window in the TOT task (6/18 participants) and during the middle and late windows in the complex tone task (7/18 and 9/18 participants, respectively).

A second set of analyses focused on the RMS and product-moment ( $Q$ ) values associated with satisfactory ECD

solutions during the middle and late time windows.  $Q$  is an estimate of the strength of the intracranial current producing the observed magnetic flux distribution at a particular point in time. Both parameters indicated a general reduction in the strength of stimulus-locked, focal neurophysiological activity during the late time window, but no significant effects involving Task or Hemisphere were present. Mean and standard deviation values are listed in Table 1.

Profiles of activity during the middle and late windows for three representative subjects are presented in Fig. 3. Predominant left STGp activation in the VOT task (represented by the number of late EF activity sources in green circles) is shown by these three as well as nearly all of the other subjects in the experiment. In contrast, late EF sources in the TOT task (yellow circles) vary in number over the left and right STGp to different degrees in each subject.

## Discussion

Elevated hemodynamic responses to speech compared to non-speech sounds (tones, noise compressed or degraded speech) have been found at three major sites within the posterior portion of the superior temporal gyrus: an area anterior to Heschl's gyrus, the supratemporal plane that extends posterior to Heschl's gyrus, and the dorsal bank of STS (Binder et al., 2000; Jäncke et al., 2002; Wise et al., 2001). Although predominant activation in one or more STGp sites in the left hemisphere has been reported by some investigators (Binder et al., 2000; Burton et al., 2000; Demonet et al., 1992; Roberts et al., 1998; Vouloumanos et al., 2001), others have failed to find hemispheric asymmetries in task-related changes in blood flow in this region (Belin et al., 2002; Jäncke et al., 2002).

Using MEG, which measures neurophysiological activity in a more direct fashion than hemodynamic imaging methods, we found evidence for bilaterally symmetric activation of STGp during the early stages of auditory processing of simple speech stimuli, and evidence for predominant activation of various left STGp sites lasting up to approximately 1400 ms after stimulus onset. Early activity was observed primarily in the vicinity of the primary auditory cortex, in and around Heschl's gyri. Later activity was found in all three major STGp subregions listed above. Based on this

Table 1  
Group mean RMS and product moment during the middle (~130 to 800 ms) and late (800 to 1400 ms) time windows

		Left hemisphere		Right hemisphere	
		Middle window	Late window	Middle window	Late window
VOT	RMS (fT)	62 (15)	29 (10)	57 (20)	28 (11)
	$Q$ (nAm)	14 (4)	7 (3)	11 (6)	8 (5)
TOT	RMS	55 (10)	18 (8)	51 (16)	15 (7)
	$Q$	11 (5)	7 (4)	13 (4)	6 (3)
Complex tones	RMS	48 (12)	17 (9)	51 (17)	14 (6)
	$Q$	10 (3)	8 (3)	9 (5)	6 (4)

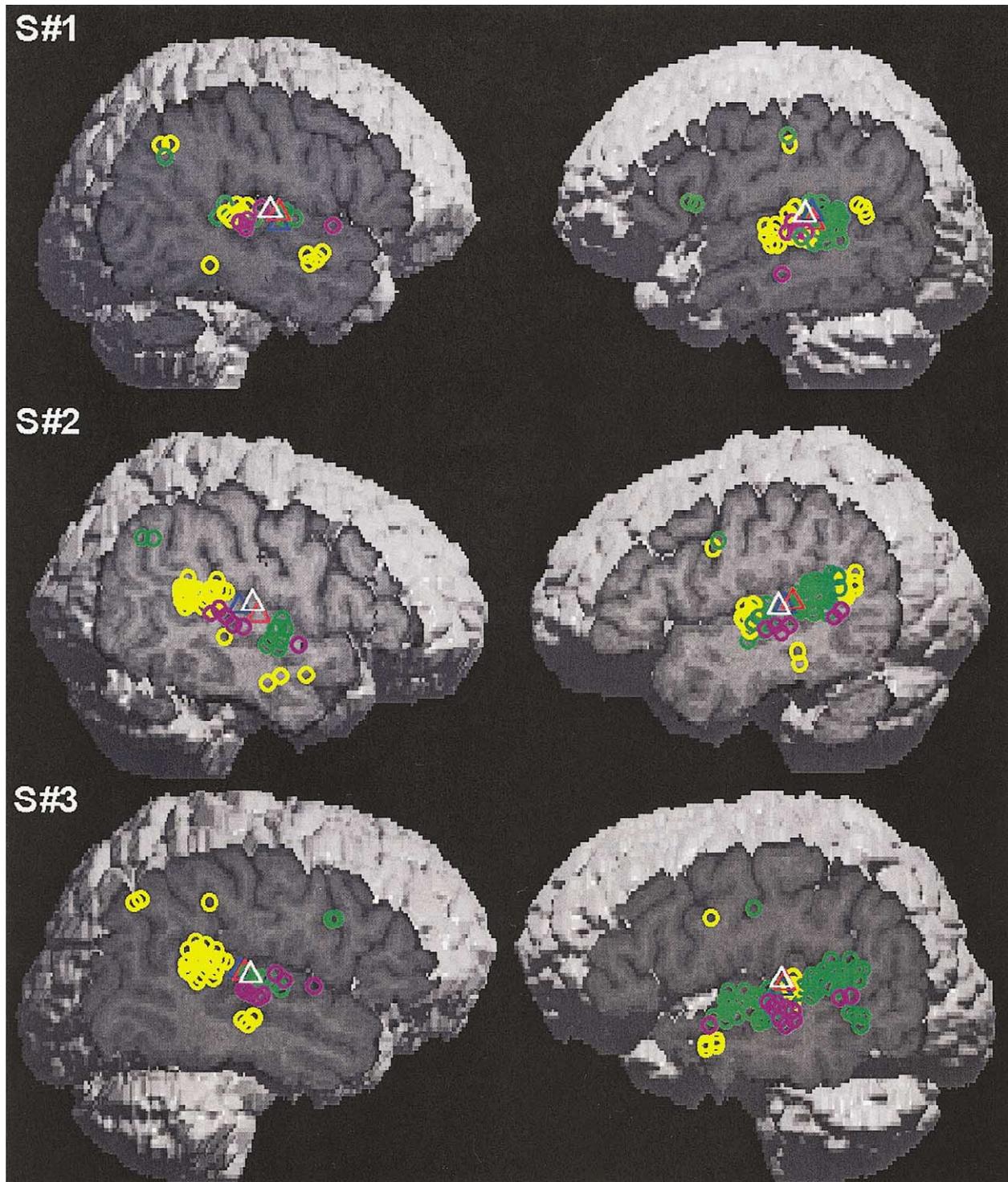


Fig. 3. Locations of activity sources during the late components of the EFs in response to speech (green circles) and nonspeech stimuli (yellow circles for TOT tokens and magenta circles for complex tones) for three representative subjects. Source locations computed at the peak of the N1m component are shown as red (speech), blue (TOT), or white (complex tones) triangles. For the MEG data slice thickness is 1 cm. Note the variety of activation profiles during in the TOT task, which contrasts sharply with the more invariable profile obtained during the VOT task.

evidence one may surmise that association cortex in the left STGp is preferentially *engaged* during processing of simple speech stimuli. However, support for the controversial claim that the left STGp is further *specialized* for the pho-

nological and/or phonetic analysis of speech stimuli would require evidence for selective activation of this area in response to speech stimuli as compared with auditory stimuli that are not perceived as speech. Two such sets of stimuli

were used in the present study. The two-tone stimuli contain a temporal acoustic cue (TOT), which is acoustically and perceptually equivalent to voice-onset time, a cue used by listeners to discriminate among voiced (/b/, /d/, /g/) and voiceless (/p/, /t/, /k/) consonants. In contrast, complex tone stimuli lack acoustic cues known to be essential for the perception of speech sounds. Although neither stimulus series can be perceived as speech, TOT tokens can be perceived categorically like voiced and voiceless consonants. Our data failed to provide strong support for the hypothesis that STGp is specialized for phonological and/or phonetic analysis of speech sounds. The number of activity sources in the left STGp during the middle window, reflecting neuronal signaling around the time that a perceptual decision regarding the identity of the stimulus is made, did not differ significantly between the VOT and TOT series. There was, however, a significant difference between speech stimuli and complex tones, suggesting that left STGp activation may require the presence of certain phonetically relevant acoustic cues that were absent from the latter stimulus series. Interestingly, there was a decline in the degree of left STGp activity, in both the middle and late windows, from speech to nonspeech analogues to complex tones. This trend cannot be accounted for by task differences in the early auditory processing associated with acoustic differences among the three stimulus sets, since activity in the early window did not reveal trends in the same direction. Therefore, linguistic context per se (speech in the VOT task, nonspeech in the TOT task) may also modulate activity in left STGp in addition to the presence of a phonetically relevant acoustic cue. This preliminary evidence may suggest that speech stimuli, even those that have no lexical referents, receive specialized processing by neurophysiological mechanisms located in the posterior part of the superior temporal gyrus.

Disagreements among previous functional brain imaging studies with respect to the degree of lateralized, speech-specific activation of STGp may be explained, at least in part, by the presence of large individual differences inflating the contribution of sampling error in the data. Inspection of individual activation profiles revealed a great degree of variability, with 10 participants showing greater activity in the VOT than in the TOT task and the remaining 8 participants showing the opposite trend. The difficulty in detecting consistent hemispheric asymmetries in the context of speech processing tasks may also be due in part to the fact that hemodynamic measures reflect underlying changes in tissue metabolism resulting from neurophysiological processes that occur both early (and appear bilaterally symmetric) and late after stimulus onset. Other contributing factors may include masking effects produced by scanner noise (in fMRI studies) (Hermann et al., 2000), problems related to the need to match stimuli in the experimental and baseline conditions (validity of the subtraction protocol), and differences among studies in image analysis procedures (e.g., whether image “flipping” is employed) (Jäncke et al., 2002).

Given the lack of major differences in the degree of activity in response to speech tokens and their two-tone analogs during the early and middle time windows, what are we to make of the different pattern that emerges during the late time window? It appears unlikely that this pattern is attributable to differences in perceptual processing per se. In a reaction time study (Pisoni and Tash, 1974), listeners were able to categorize synthetic VOT stimuli accurately in under 600 ms, and in even less time when the stimuli were highly unambiguous series-endpoint stimuli (such as those used to elicit the evoked magnetic fields recorded in the present study). Because these reaction times reflect both perceptual processing and response selection and execution, the actual perceptual processing times are no doubt considerably shorter still. Thus, we can assume that by the beginning of the late time window in the present study (i.e., 800 ms post-stimulus onset), perceptual processing of a given stimulus was essentially complete. One possible explanation for these results is that the left STGp remains more active for the VOT task during the late time window to support continued activation of the representation of the speech stimuli in working memory. Recall that during the VOT, TOT, and complex tone tasks, participants heard stimulus pairs and decided if the two items were the same or different. The brain activity reported and analyzed in this study was recorded as participants heard the first member of a stimulus pair and awaited presentation of a second member. The continued activation of the left STGp during the late window may reflect the operation of a covert rehearsal process, or “articulatory loop” in working memory (Baddeley, 1986), perhaps in tandem with prefrontal areas, to support the continued representation of such stimuli and thereby facilitate comparisons with subsequently presented stimuli. Such a memory rehearsal process is known to be specific to speech, at least among auditory stimuli, which would explain why the continued activation of the left STGp was not observed for the TOT stimuli (Kim et al., 2002; Schweitzer et al., 2000). Moreover, sustained electrophysiological activity that lasts for several seconds in various lateral temporal lobe sites has been found during intracranial recordings in patients performing working memory tasks (Ojemann and Schoenfield-McNeill, 1999).

Hemisphere differences in the field strength of the N1m component in response to speech stimuli (vowels) may depend on specific task demands (Poeppel et al., 1996). In general, however, brain activity represented by the early component of the EF appears to be similar in response to both speech and nonspeech stimuli, with differences being apparent only during later processing (e.g., Eulitz et al., 1995). In fact, evidence from a series of earlier MEG studies suggests that systematic variations in the intensity of N1m activity in response to the VOT and TOT series used in the present study are virtually identical for speech and nonspeech stimuli (Simos et al., 1998b,c). Interestingly, changes in the N1m amplitude paralleled the perceptual identification functions displayed by the same participants.

Modulation of the amplitude of the magnetic mismatch field, which occurs slightly later than the N1m response and originates in the vicinity of the primary auditory cortex in the supratemporal plane, may also reflect phonetic disfunctions (Phillips et al., 2000). In the present study, while early activity was essentially bilaterally equivalent for both speech and nonspeech stimuli, we did observe greater magnetic flux amplitude in response to the TOT compared with the VOT stimuli. The differences in overall activation between the speech and nonspeech conditions may reflect acoustic differences between the two sets of stimuli. It is unlikely that the modulation of N1m field strength was due in any way to stimulus-related effects in other measures of brain activity that were observed during the later portions of the EF. Not only did the profile of the early effects on N1m RMS not match the profiles of later stimulus-specific changes (e.g., in terms of laterality), but the former were also in the opposite direction compared with the latter.

In sum, current findings suggest the presence of an area in the left STGp that is involved in phonological and/or phonetic processing. This area may also be involved, to some extent, in processing of nonspeech stimuli containing cues analogous to speech stimuli. Activity in this region is weakened when the auditory stimuli do not contain speech-like acoustic cues. Given the evidence for some involvement of this area previously thought to be specialized for speech in nonspeech processing, it would be of interest to manipulate the acoustic characteristics of nonspeech stimuli to determine under what conditions the latter components become active.

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